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THE PEDIATRICIAN IN THE COUNCILS OF THE NATION

PRESIDENT'S ADDRESS

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The present controversy concerning the adequate provision of medical care warrants rather particular emphasis on the well recognized responsibilities and early aims of the medical profession in general and on the record of the successful accomplishment of those aims.

For pediatricians in particular two conditions have arisen which call for discussion. First, the pediatrician's field of practice seems to be somewhat in jeopardy because of a decrease in the birth rate and the better equipment of the general practitioner to care for infants and children. Second, there is a need for better training of the student and more interest on the part of the practitioner in the care of the convalescent and chronically ill child.

This is the fifty-second time that the members of the American Pediatric Society have been asked to listen to the considered opinions of the one of its number who has been given the great honor of acting as president. But never before, according to the record, have they been asked to listen to a postmortem—a pediatric postmortem—presidential address. For fifteen months, immersion in the socioeconomic aspects of medicine, public health education and dissemination of health information in general have replaced for me the practice of pediatrics in the hall bedroom and hospital ward. Unbalanced budgets, rather than unbalanced diets, committee meetings, rather than staff conferences, have occupied my thoughts, so that my classification as emeritus pediatrician rather than my selection as president of this society would seem more suited to my deserts. For this reason, I am all the more appreciative of the graciousness shown me.

The medical profession has been invited to take the witness stand and explain itself to a somewhat misinformed and skilfully prejudiced jury.

Read at the annual meeting of the American Pediatric Society, Skytop, Pa., May 2, 1940.

As the man who made the sidewalks of New York famous has so frequently said, "Let's look at the record"—the record of the aims of the American Pediatric Society, as representative of American medicine, and the record of what has been done toward the accomplishment of these aims.

The record began with the first presidential address, delivered by Abraham Jacobi in Washington, in 1889. Parenthetically, it should be admitted that that address has furnished ideas and material for a majority of its successors, with emphasis on that of 1940. In it was said:

> Questions of public hygiene and medicine are both professional and social. Thus, every physician is by destiny a political being; viz., a citizen of the commonwealth with many rights and responsibilities.

These rights, opportunities and responsibilities have been recognized by the American Pediatric Society since its creation and have occupied as much of the society's considerations as have the purely academic interests of its membership. The society's part in the "councils of the nation" has been dominant in effecting those advances in the science and art of medicine which have established here the most healthful living conditions of any nation in the world.

How widely some of the members have spread their influence is shown by Jacobi's introduction to Nascher's book on geriatrics. Here he said:

> Fortunately the interest of the last fifty years in pediatrics has not built up a new specialty with all its narrowing influences. It has broadened the horizon of honest students and made better general practitioners.
>
> I am sure that the pediatrician cannot succeed in his practical work without being a student of nosology in general. On the other hand, I am sure that the internist and the general practitioner does not, without at the same time being a pediatrist, reached a standard by which he may be of real use at the bedside or the councils of the nation.

Thus one can turn to literature dealing with the medical problems of old age, geriatrics, for evidence that those physicians dealing with disease and treatment in infancy and youth, pediatrics, have done their part in assuming the position which the medical profession has striven for and succeeded in maintaining, certain legal authority to the contrary notwithstanding.

This introduction further stressed the importance of broad-mindedness even in the specialties and recognition by all classes of physicians of the opportunities peculiarly open to them for service as political beings.

One is urged to accept the belief, and Jacobi's own activities illustrated the point fully, that a pediatrician must not become a pediatrician too early or be one too exclusively in his medical career. He thus decried the idea that pediatricians hold the only key to the nursery and

with it lock themselves in and others out. He put the same emphasis on the physician's responsibility toward national health as he did on his responsibilities toward the health of the patients in his own consulting room.

In the early days it was thought advisable—now it has become necessary—for the pediatrician to take over the responsibility of the whole child. This is true not only of medical care but recently even more of those phases of the child's socioeconomic existence over which government has supposed supervision. In the performance of such supervision, a government certainly needs the advice which only a comprehensively trained medical man can give.

One wonders if Jacobi, at the time of writing that introductory chapter, foresaw anything of the present attempt to supplant by politically controlled bureaus the free use of the medical profession's own abilities along health lines. One wonders whether he expected to hear the medical profession's contributions toward improvement in the nation's health described as "restraint of trade."

The record plainly shows the early awareness of the members of the society of the opportunities open to them in so many different directions. After surveying what has been done toward the fulfilment of those opportunities, I shall hazard a suggestion which may further increase the efficiency and services of the physician to the community in which he lives.

THE PEDIATRICIAN AS AN EDUCATOR

Jacobi would have had the physician, and particularly that one who makes pediatrics his special study, a pedagogue by profession, a leader and teacher of the young, interested in and with authority over the health aspects of education.

Physicians have been that. Committees of physicians, working without remuneration, have studied the problems of education, with results that would have been slow in arriving under any other stimulus.

In larger centers of population medical officers and teachers have been found no better fitted for their work than the proverbial New England schoolmarm was to teach calculus or to appreciate the importance of malnutrition or susceptibility to disease.

Budgets have been found showing large sums spent yearly on substitute wages for teachers absent on falsified sick certificates. Many a needed innovation could have been supported on the money wasted on special classes for the handicapped child, classes created unnecessarily and mainly for the added stipend attached thereto.

A study of the special class was made in 1930 by the Research Association of Teachers' College, Columbia University. It was expected to find that much was being done by this means to reduce the number of

physically and mentally handicapped children. The fact was, however, that where there were the most special classes there also were the most handicapped children. This was not because the interest in the special class brought the children into the light, but rather because the classes were padded and poorly run. The handicapped children received little, if any, relief. Their numbers were augmented by persons whose right to a place in a special class was questionable.

Last spring, nine years later, thirty long-suffering pediatricians visited two hundred and forty so-called "outdoor classes," with the object of appraising them from a purely medical standpoint. These schools were scattered over five counties of a large metropolitan area. It was a fair cross section of other such areas. Although the classes were small and the teachers were selected for their supposed interest in school health, there was little appreciation of the problems presented, either medical or social; diagnoses for admission were frequently erroneous and did not justify the establishment of special classes—carious teeth, flatfoot and adenoids, for example. There were no standards for discharge. The rooms were not open air—they were cold air rooms. The children were not open air children—they were pale, cold, dead air children.

Such conditions are not of medical origin, but their correction has been the task of medical men on advisory boards. False certification of physical fitness of teachers cost one city over a million dollars in one year, and this condition was exposed but not as boldly as it should have been. An adequate staff of medical examiners for schools was suggested to replace the single examiner who for each two or three minute examination had been paid 25 cents. Full time medical staffs were created which, cooperating with the local physician, really accomplished health education of both child and family. Prompt grading of retarded children on determination of their chronologic and mental age was recommended and adopted to eliminate the customary waste of three years before change had been allowed. The special needs of school children in poor condition were early recognized, and segregation when needed was accomplished, with particular emphasis on maintaining, as far as possible, normal surroundings. Under medical commissions, scientifically adjusted supplementary nourishment at school and dietary education at the same time at home were instituted. Rest took the place of isolation; treatment replaced inhibition.

These conditions are of bureaucratic origin; the diagnosis and treatment have been by the medical profession. The physician has proved himself a pedagogue, a modern pedagogue; he has even been discovered publicly discussing the relative merits of progressive and formal education.

It seems plain that in the provision for the physical health of the school child the medical profession has done its part. Education is at least on its way toward a bettered physical setting.

MENTAL HYGIENE IN CHILDHOOD

There is another opportunity which has been recognized and finally seized with avidity by the pediatrician. That is the matter of the mental health and psychologic comfort of the infant and child, as well as the peace of mind of the parent, nurse and teacher. The record of this society is full of references to and suggestions about this phase of the physician's responsibility. Members of the society have been told by those who have had much to do with its activities that the pediatrician should have as much interest in mental as in physical hygiene, told the first time in 1889. The source is obvious. Since then, the question of the relation between early functional nervous disorders and later mental disease has been a frequent source of disagreement. The members have been told by some that mental invalidism has been considered to result directly from neglect of the psychologic interests of childhood and by others that faulty human relationships are the basis for all delinquencies.

The theory that a problem child becomes a problem child only when his environment has become a problem has been offered as clearing the way to a therapeutic approach, and this view is supported by recently produced evidence showing that in one large clinic the incidence of failures in the parent-child relation and all their attendant consequences was even greater than that of purely medical pediatric problems.

Discussions have been frequent as to the relative importance of heritage and environment in the formation of character and of the significance of the fact that heritage is fixed and beyond control but that environment is created and entirely controllable by those with authority over the child's life.

Emphasis has been laid on the lack of proper instruction in the functional nervous disturbances of childhood. In 1931 it was reported that such instruction was offered in only half of the nation's schools, this lack applying even to the study of the formation of habits.

The term "psychiatrically minded pediatrician" was coined by one physician in calling attention to an important branch of medicine too little thought of by the children's doctor.

One may find it difficult to accept as proved the statement that "later adjustments of the adult to the social group are largely dependent on the development of satisfactory behavior patterns in early childhood." The pediatrician should, however, accept the responsibility that rests squarely on his shoulders of educating parents, nurses and teachers in such matters as the avoidance of overcontrol and in the value of guarded scientific neglect of as many as possible of the minor errors of conduct. The one, overcontrol, deprives the child of the unhampered acquirement

of wisdom through experience; the other, selective reproof, emphasizes the importance of interpreting behavior as well as judging conduct. Neuroses arise in childhood as often from nagging and repeated negations as from neglect and are as common to the child born to luxury as to the one in the most underprivileged class.

Disturbances in digestion and nutrition will serve as an example. Difficulties of this sort in the first years of life are less often due to organic than to functional causes. The method of administration more often than the food itself is the cause of digestive trouble in childhood.

Recognition of the importance of and response to these demands on the pediatrician's attention has been slow, perhaps naturally so, as they are time-consuming and cannot be determined through the use of instruments of precision. They are, however, of importance, because children have anxieties just as do adults. Pediatricians are learning to apply to their specialty the statement of Barrow, that "anxiety arises from many sources, and such as is not released by action often expresses itself in disease." This describes the constantly frustrated child. I am paraphrasing, for my own use, Bannister's statement that what one needs to teach children is the art of living and what one should first let them find out for themselves is how to avoid the anxiety that results from error.

The best source of information along this line is not to be found in psychiatry but rather is the natural product of the many studies now being carried on in the structural, functional and intellectual growth and development of the normal child.

These studies have shown that there is a normal variation in the time of appearance and sequence of all developmental progress; there is an optimal time or period for the acquirement of each new capacity. Appreciation of the responsibility to provide adequate and timely outlets for these new abilities is important, for by it one avoids the error of forcing children ahead of nature's schedule and the mistake of undue apprehension in instances of delayed advance.

What has been done by the joint efforts of the psychiatrist and pediatrician along this line may best be shown by the results of a study of cases of delinquency and maladjustment brought before the children's and domestic relations courts. As the result of the recommendations made, one-half as many children now go before the bench as did when the causes of the difficulties were less well understood. The management is now corrective rather than punitive.

Holt's forecast is being verified—physicians are recognizing the importance of mental hygiene early rather than after the later sequelae have appeared. Is this not evidence that the profession is meeting its responsibilities?

PHILOSOPHY OF THE PHYSICIAN

I have referred to the improvement of the physical and mental welfare of the school child as illustrative of the fundamental importance of the things that the medical profession has wanted to do and has done. In spite of all this the medical profession seems to be misunderstood, perhaps deliberately. It may be because physicians are admittedly poor business men. The philosophy of the profession as a whole is, and probably always has been, difficult for the "hard-boiled" lay mind to appreciate. Individual or collective altruism has always been subject to suspicion and misinterpretation. The connotations of "quid" and "quo" to the physician are not always the same as to the public. However, one must not forget that unless that same lay mind had in many instances initiated and supported the work of the physician, his work would never have been done.

The physician expects to do a large part of his work without pay, and yet he looks down on the thought of a retainer's fee in advance or legal aid in collecting fees for services rendered.

The responsibility of the physician is, rightly, to discover and eliminate the causes of sickness and death, and yet it is commonly said of the physician that he must live by treatment of the very conditions which he strives to destroy.

One half of the national outlay for health goes to hospitals, and this half is paid before the physician's bill, yet a place on the hospital staff is the goal of every physician, although the duties are time-consuming and are not, at least directly remunerative. All this must seem funny to the efficiency expert.

The physician has always had to accept restraint. The law of the Egyptians insisted, on pain of death, that the physician should diagnose and treat all illnesses according to standards laid down. A treatment once begun had to be continued without change for at least four days regardless of symptoms. They had time to build several pyramids before this practice disappeared. Certain relics of such absurdities have persisted or comparable new ones have arisen ever since.

Control by state boards of the form and sequence of medical education and licensure, constructive for the most part, will, if overdone, handicap the teaching of medicine. State control of the hospitalization and treatment of the sick may have the same result as that so well demonstrated during the time that the therapeutic value of alcohol was determined for the physician.

Regimentation by a group of supposed experts on the cost of medical care would deprive both physician and patient of the right of free action as regards health. Finally, the physician finds himself actually in jeopardy of fine and imprisonment for not having provided health sanctuary for the inhabitants of every square foot of urban and suburban

territory. He would be condemned for not doing better what he had already done well for his community, greatly to his own cost.

Few attempts of any sort to improve man's ability to live healthfully in his surroundings have been free from man-made interference. The pediatrician of today, however, seems to be facing certain more specific obstacles arising from natural causes.

PEDIATRIC HANDICAPS AND NEW OPPORTUNITIES

Population trends are raising questions hard for the struggling pediatrician to answer. With the reduced birth rate, only partly compensated for by a lower infant mortality, and with specific treatment for an increasing number of diseases that have formerly taken toll of early adult life, the pediatrician seems to be passing, as has been said, out of the field of pediatrics into the realm of geriatrics. A new kind of responsibility faces the pediatrician of the future. Planned parenthood and economic obstacles to marriage threaten a reduction by 50 per cent in the population of those members under the age of 20 years and an increase in nonproducers over the age of 60. Life control cannot be applied to geriatrics as has birth control to pediatrics, although euthanasia may be just around the corner.

Because of all this, it is just so much more the pediatrician's responsibility to conserve the diminishing supply of dependable youth and to make it more dependable. It must never be said of this country that the United States is "the one civilized nation in which coffins are more numerous than cradles."

To what can one look forward as a substitute for the spectacular advances made by such students as Roach, Holt, Griffith and Morse in the control of infant and child mortality from gastrointestinal causes? Deficiency diseases offer an opportunity perhaps as great. The story of the evolution of chemotherapy may be as dramatic when it is all told.

There is one subject, however, that has been recently termed "medicine's forgotten man." It is an exceedingly inclusive subject. It combines and will have accomplished when it has been fairly settled: a contribution to public health education, an immediate application of preventive medicine, economy in hospital and home care for both physician and patient and a definite effect on the number and condition of the chronically ill. The unity of these objectives has already been referred to by Carpenter and Hamill, when they spoke of the close relation of preventive medicine, convalescent care and chronic illness.

The subject is convalescent care—care of the patient who is no longer acutely ill but is not yet altogether well. These patients have certainly been pediatrics' forgotten children. Students are taught now to diagnose disease and to recognize the disappearance of its signs and symptoms. Hospital wards are filled with children who are interesting just so long as they furnish material for such study and observation. Interns and

residents are eager to sign the discharge note, and parents clamor for their children's return as soon as they may be safely moved. One might remark that instructions go with the patient. So they may, but of what use is a prescription without continued knowledge by its writer of the manner of its administration and its effects? I am not forgetting the outpatient or follow-up clinics but I am suggesting that both can furnish information as to the end results chiefly and add too little knowledge of the stages through which the convalescent must pass en route to permanent cure.

An interest in and provision for real convalescent care would benefit three classes of patients: those who should not so soon have left the hospital, those who need continued medical guidance at home and, especially, those who themselves would profit by and would contribute to medical knowledge by residence in a convalescent hospital, not a "convalescent home."

Chronic illness of necessity begins during convalescence from acute illness. There is not enough provision for or interest in the care of the chronically ill. Only municipal hospitals *have* to accept chronically ill patients. Why should not every hospital find time and space to study as intensively as is done in acute illness the means by which these patients may be made less ill, less dependent, less of a handicap to the efficiency of those who must care for them?

Is there not an opportunity here to avoid relapse and complication, and does any physician now feel as well posted on the emergencies that may arise in convalescence or chronic illness as on those in acute illness? Convalescence in children's illnesses is as varied in requirement as are the acute diseases from which it arises. The difficulties are not all somatic, and the accompanying disturbance to the mind is an equally important present problem and future menace.

A recent conference of the best medical minds of the East brought out many interesting things concerning convalescent needs but demonstrated at the same time too forcibly the fact that what was known was more theoretic than factual and that provisions for the study of convalescent care were sadly lacking.

There may be a fruitful field for expansion by the pediatric student, teacher and practitioner in that period between the cure of disease and recovery from its indirect constitutional effects. These effects are both medical and economic.

In the office of the Committee on Public Health Relations at the New York Academy of Medicine there stands a small figure which to me accurately illustrates today's convalescent needs. The inscription on this statuette is "Discharged Cured." The figure is that of a stooping, tired man, whose recently sterilized clothes hang shapeless on a somewhat emaciated frame; his coat collar is turned up, concealing the absence of a shirt underneath; his features are sharp and wan, showing

the results of recent illness, an illness whose effects on him constitutionally have by no means been neutralized; his small belongings are carried in a knotted handkerchief, his pockets are empty and his old hat partially conceals an unkempt overgrowth of graying hair. Here one has the outward, tangible evidence of a great need long recognized and of a great responsibility up to the present impossible of acceptance.

"Discharged cured!" Cured of what—of disease only or of its effects also? Is he able only to dress and leave the hospital? Is he able barely to take care of himself while another works for his support? Is he able only quickly or ultimately to fall victim to relapse or, through reduced resistance, to a new disease?

The term convalescence does not mean that care is no longer important. It should indeed emphasize the imminent need of another type of care. Convalescent care is as much a part of permanent cure as is the actual application of medical or surgical procedures to infection.

There comes a time in all illness, whether acute or chronic, when the patient can get no better by lying in a ward bed or sitting in a wheel chair. This stage in the progress of treatment does not necessarily or usually coincide with ability on the part of the patient to care for himself, much less to resume his share of responsibility toward others. Both mind and body need release from the restrictions and limitations of hospital life. This point in the progress of disease, whether chronic or acute, represents a critical period in treatment, and only by suitable provision for this critical period can permanency for what has been accomplished in the hospital be assured.

True economy in hospital care is always directly proportionate to the completeness and permanence of release both from disease and from the subsequent effects of that disease. The difference between lasting cure and relapse with resultant dependence may be largely controlled by a relatively short period of properly conducted care after the patient has left the hospital.

I confidently look forward to another statuette, again labeled "discharged cured." It may represent a child or an adult, but in either case, it will denote a job completely done, a discharged patient ready for a normal existence.

Here is an opportunity that may prove as fruitful as did that offered by the problem of infant feeding. It is to be hoped that to solve the problem of convalescent care it will not be necessary to pass through the algebraic agony that marked the change in infant feeding from giving top milk to prescribing canned concentrate.

With the change of one word one may say of convalescence what has been said of inherited disease:

"We have much to learn along these lines, and some day the pediatrician may be able to prove that even in chronic disease he is a practitioner of the healing art."

CALIFORNIA TALL CHILDREN

ORREN LLOYD-JONES, M.D., PH.D.
LOS ANGELES

In California the opinion is often expressed by teachers of physical education, athletic coaches and pediatricians as well as by travelers and writers less qualified to judge, that children in that state exceed in weight and stature those of like age in Eastern and Central states. The implication is that there is something in the living conditions in California that serves as a stimulus for extra growth. The question arises: Is there any factual basis for these opinions, or are they merely the expressions of an overenthusiastic local loyalty said to be characteristic of Californians?

An opportunity was offered in 1937 to submit the matter to statistical investigation. With the help of the WPA and under the sponsorship of the Board of Education, a supplementary project for school health aid had been organized under the guidance of Dr. Sven Lokrantz, director of the health section. Workers were carefully selected on the basis of their general understanding of, and their accuracy in, measuring and recording. They were coached specifically for the work of weighing and measuring the children and of recording those measurements and other pertinent facts. In elementary schools shoes, coats and heavy sweaters were removed from the children before the weighing. In junior and senior high schools only gymnasium trunks and blouses were worn during the weighing. All heights were taken with the children in stocking feet. Other data recorded for each child included name, race, birth date, birthplace and date of coming to California. In the assembling of the data, age was counted from the nearest birthday. Pounds and inches were recorded to the nearest quarter.

These data permit the possible influence of California environment on growth to be examined in the following three ways:

1. Comparison of the average heights per age of Los Angeles school children with similar averages of children from other districts (tables 1 and 2).

2. Comparison of the average heights per age of Los Angeles children born in California with those of Los Angeles children born elsewhere (table 3).

3. Considering by themselves the children born elsewhere, comparison of the average heights per age among groups of any given age

who have lived in California (1) less than five years, (2) from five to ten years and (3) over ten years.

In the following discussion little mention is made of weight. All tables have been worked up for weight as well as for height, but for the purpose in hand, study of the data on weight merely confirms the conclusions based on heights. Therefore, solely in the interest of economy of space these figures are here omitted.

LOS ANGELES CHILDREN COMPARED WITH THOSE OF OTHER DISTRICTS

Tables 1 and 2 show the average heights by age of the Los Angeles children along with those of other groups selected for comparison. For

TABLE 1.—*Average Heights (Inches) for Age: Boys*

Age (Years)	Los Angeles 1938*	Gifted Children 1923		San Francisco 1923		Oakland 1893		All Sections of U. S. 1923	
		Height	Deviation	Height	Deviation	Height	Deviation	Height	Deviation
6	46.0	....	.....	....	.....	44.1	—1.9	45.2	—0.8
7	48.2	48.5	+0.3	47.1	—1.1	45.0	—3.2	47.0	—1.2
8	50.4	50.5	+0.1	49.2	—1.2	47.6	—2.8	49.3	—1.1
9	52.5	52.3	—0.2	51.2	—1.3	49.3	—3.2	51.3	—1.2
10	54.4	53.7	—0.7	53.3	—1.1	51.9	—2.5	53.2	—1.2
11	56.3	56.2	—0.1	54.7	—1.6	53.5	—2.8	55.1	—1.2
12	58.3	57.9	—0.4	56.9	—1.4	55.1	—3.2	56.8	—1.5
13	60.6	59.9	—0.7	58.8	—1.8	56.8	—3.8	59.1	—1.5
14	63.3	62.6	—0.7	61.4	—1.9	59.7	—3.6	61.2	—2.1
15	65.5	64.7	—0.8	62.8	—2.7	61.8	—3.7	....	.....
16	67.3	....	.....	....	.....	64.5	—2.8	....	.....
17	68.1	....	.....	....	.....	67.1	—1.0	....	.....
18	68.6	....	.....	....	.....	67.6	—1.0	....	.....

* Dates show when measurements were made.
† Deviations are from Los Angeles values.

ease in quick comparison the deviations from the Los Angeles values are also set down.

One is struck at once by the fact that with the exception of two figures, the deviations are all minus. An extensive search of the published data on stature of public school children in the United States was made, and no group was discovered showing statures or weights for age equal to those of the Los Angeles children. Gray and Nicholson [1] have collected and published records of private school boys who showed statures superior to those reported here, but being select groups they are not included in this study. The public school children chosen for comparison with the Los Angeles children in this series made up three California groups and one composite group from various sections of the United States.

1. Gray, H., and Nicholson, S. T.: The Tallest American Boys, J. A. M. A. **88**:2022 (June 25) 1927.

The "gifted children" included in tables 1 and 2 comprise the 643 subjects selected by Terman [2] on the basis of superior general intelligence and serving as the foundation for his celebrated "Studies of Genetic Genius;" they were chosen from California schools, 285 of them from Los Angeles schools. They were studied anthropometrically by Baldwin (published in Terman [2]), who found them in stature and weight, as well as in several other physical attributes, well in the lead of any children reported on in published records of the time. In fact, the figures show them even taller at the ages of 7 and 8 than the Los Angeles children of the present series; but at all other ages, their averages fall definitely below the Los Angeles averages based on purely random sampling. The birthplace and the number of years these children had resided in Cali-

TABLE 2.—*Average Heights (Inches) for Age: Girls*

		Gifted Children 1923		San Francisco 1924		Oakland 1898		All Sections of U. S. 1923	
Age	Los Angeles 1938*	Height	Deviation†	Height	Deviation	Height	Deviation	Height	Deviation
6	45.7	....	.....	....	.....	44.4	—1.3	44.8	—0.9
7	48.0	47.5	—0.5	46.9	—1.1	44.9	—3.1	46.7	—1.3
8	50.2	50.0	—0.2	48.3	—1.9	46.8	—3.4	48.9	—1.3
9	52.1	52.3	+0.2	50.9	—1.2	49.2	—2.9	50.9	—1.2
10	54.3	53.6	—0.7	52.7	—1.6	51.5	—2.8	52.9	—1.4
11	56.6	56.5	—0.1	55.0	—1.6	53.9	—2.7	55.2	—1.4
12	59.2	58.0	—1.2	57.3	—1.9	56.6	—2.6	57.5	—1.7
13	61.3	61.1	—0.2	59.4	—1.9	60.0	—1.3	59.8	—1.5
14	62.6	62.3	—0.3	60.7	—1.9	61.2	—1.4	61.2	—1.4
15	63.4	64.0	+0.6	61.3	—2.1	61.9	—1.5	....	.....
16	63.7	....	.....	....	.....	62.7	—1.0	....	.....
17	63.8	....	.....	....	.....	62.7	—1.1	....	.....
18	63.7	....	.....	....	.....	63.2	—0.5	....	.....

* Dates show when measurements were made.
† Deviations are from Los Angeles standards.

fornia are not given in Baldwin's report. A certain amount of racial selection is suggested, however, from the fact that about 67 per cent of the grandparents were English, Scotch, German or Irish, all races at the tall end of the racial series.

The San Francisco children are a portion (7,463) of those studied by Faber. These figures on them were reported by Baldwin [2] in connection with his studies of the gifted children referred to. The Los Angeles children at each age are well over 1 inch (2.54 cm.) the taller (the average height of the Los Angeles group is 1.6 inches [4.06 cm.] taller). Is this considerable difference in children's heights seen in two California cities to be accepted as a measure of extra growth in the southern city? Certainly not entirely so, for there was an interval of

2. Terman, L. M.: Genetic Studies of Genius, Stanford University, Calif., Stanford University Press, 1925, vol. 1.

about fifteen years between the two studies; people may have learned how to grow children faster since 1923. That this time element is probably an important factor is indicated when the figures for Oakland children measured in 1893 are considered.

These Oakland records were taken under the direction of the University of California and Stanford University, under the supervision of Professor Earl Barnes of the latter institution. Six thousand children were measured in the fall of 1892, and there is every evidence that the work was done with precision and accuracy. Comparisons with the figures for the Los Angeles children are startling: The average deviation between the two series is about 3 inches (7.62 cm.). Here it would seem highly probable that the element of forty-five years' history must weigh more heavily than that of geography, climate or any other environmental factor. A similar comment can be made of the comparison of the figures of Faber for San Francisco (1923) with those of Barnes for Oakland (1893). The children examined by the latter author are about 1.5 inches (3.81 cm.) the shorter, and obviously a strip of bay water cannot account for a difference of almost 1½ inches in stature among the school children of two cities so alike in other respects. Yet in 1893 Oakland had nothing to be ashamed of, for, as Professor Barnes pointed out in his report, when these figures were shown at the Chicago World's Fair in comparison with returns from a half dozen Eastern cities, "The result was very flattering to California's pride as the Oakland children were taller and heavier than the children in any of these other cities." [3] It would be surprising indeed if the improvements in diet, in hygiene and in pediatric knowledge during the past forty-five years (fifteen years in the case of Faber's work) had not influenced rate of growth in children.

Finally, the most recently published data dealing with the height of children in various sections of the United States were considered. Palmer and Collins' [4] paper, published in 1935, was based on measurements taken between 1922 and 1924, and the data are thus strictly contemporary with those of Faber (San Francisco). These data of Palmer and Collins are perhaps the most carefully collected of any available on the subject. Detailed plans for the entire study were deliberately laid out, and personnel from the army medical staff was sent into each district for the specific purpose of taking the measurements. Schools were chosen in four sections of the country, Northeastern, North Central, South Central and Western, and about 9,000

3. Barnes, E.: Oakland School Report, no. 92, 1892-1893, p. 38.

4. Palmer, C. E., and Collins, S. D.: Variations in Physique and Growth of Children in Different Geographic Regions of the United States: Physical Measurement Studies, Pub. Health Rep. **50**:335, 1935.

children were measured in each. The Western section, however, was confined to cities in Utah and Nevada, and only 2,000 children were included. The sections differed but slightly, but there was a perceptible tendency for Northeastern children to excel in height and weight. It is also interesting to note that the "Western" children (Nevada and Utah alone) tended to be the shortest. The figures from that report which are used in this study represent the average heights of all four sections. When they are compared with the average heights of Los Angeles children (tables 1 and 2, last two columns) the former are uniformly shorter; all deviations are minus. It is regrettable that the fine work of Baldwin and Wood [5] which served as the basis for their celebrated height-weight-age tables cannot be considered in this comparison, but because of the manner in which the data are set up (no frequencies are given) it is impossible to calculate average heights for age of the children measured.

LOS ANGELES CHILDREN: COMPARISON OF THOSE BORN IN CALIFORNIA AND THOSE BORN ELSEWHERE

Thus it is seen that by comparison with other existing data it is impossible to evaluate satisfactorily the precise effects of California environment on growth. This is true because even the most recent data available antedate the data of this series by fourteen years. Therefore, all such comparisons are subject to the criticism that any differences revealed may be due to improvements in care and nutrition, made possible by newer knowledge. This newer knowledge is widespread, and therefore it is easy to confuse regional with chronologic factors. Bowles [6] has shown, for example, that even among adults there has been a slow but constant rise in the stature of American people; if exact data were available, probably every decade would show its own slight increase. For Harvard students during the past sixty year period this increase has been at the rate of 1 inch (2.54 cm.) every thirty-two years. Moreover, Bowles showed convincingly that this increase in adult stature is a world-wide phenomenon; he cited figures from eight European countries and from Japan in support of this idea. Whether the increase has any genetic basis or is merely a somatic expression of worldwide economic and social progress is less easy to prove. Thus, in comparisons of the influence of various environments on growth, the data to be strictly comparable must be strictly contemporary.

It was possible, however, to derive from the figures in the present series some evidence on environmental influence which was based on

5. Baldwin, B., and Wood, T.: American Child Health Association, 1923.

6. Bowles, G. T.: New Types of Old Americans, Cambridge, Mass., Harvard University Press, 1932.

data that were not only strictly contemporary but at the same time free from any differences such as those in ways of selecting material and in methods of recording which may have existed in other studies. This evidence was derived by separating the Los Angeles children into two series: (1) those born in California and (2) those born elsewhere. There were available for this comparison 73,248 children born in California and 40,038 born elsewhere. The latter group had of course dwelt in California for varying lengths of time, but certainly all of them had enjoyed a less prolonged effect of California environment than had the group born in California. As a matter of fact, about 40 per cent of the group born elsewhere had lived in the state five years or less.

TABLE 3.—*Average Heights (Inches) by Age of Los Angeles Children, Comparing the Children Born in California with Those Born Elsewhere* *

	Boys			Girls		
	Height			Height		
Age (Years)	Born in California	Born Elsewhere	Deviation	Born in California	Born Elsewhere	Deviation
5	44.2	44.0	−0.2	43.9	43.3	−0.6
6	46.0	45.9	−0.1	45.7	45.4	−0.2
7	48.3	48.1	−0.2	48.0	47.7	−0.3
8	50.5	50.2	−0.3	50.3	49.9	−0.4
9	52.6	52.4	−0.2	52.3	52.0	−0.3
10	54.6	54.2	−0.4	54.5	54.0	−0.5
11	56.5	56.0	−0.5	56.7	56.5	−0.2
12	58.5	58.0	−0.5	59.4	58.7	−0.7
13	60.8	60.4	−0.4	61.4	61.0	−0.4
14	63.5	63.0	−0.5	62.8	62.6	−0.2
15	65.7	65.3	−0.4	63.6	63.2	−0.4
16	67.6	66.9	−0.7	63.9	63.4	−0.5
17	68.5	67.9	−0.6	64.0	63.6	−0.4
18	69.0	68.3	−0.7	64.0	63.5	−0.5

* Measurements are included on 37,058 boys and 36,290 girls born in California; on 19,977 boys and 20,061 girls born elsewhere.

The data arranged thus are shown in table 3. The amounts by which the children born elsewhere differ from those born in California are shown as deviations. The children born in California are taller at every age, the average superiority being about ½ inch (1.27 cm.). These results furnish rather emphatic support for the idea that the differences shown in tables 1 and 2 are at least in some degree a result of California environment and that they cannot be explained on the basis of racial selection, improved nutrition and care or differences in methods of measurement, of recording the age or of "rounding the figures" (that is, dropping or adding fractional pounds or inches), because all of these factors operated in exactly equal degree in both series.

COMPARISONS AMONG THE CHILDREN BORN ELSEWHERE

This striking superiority in height of the children born in California suggests a further division of the data on the group born elsewhere.

If in truth conditions in California are acting as any special influence to cause increased growth, this influence must be working constantly though slowly. Its effect should be cumulative, year by year, as the growing child is subjected to it for a longer time. A method for securing evidence concerning such a possible cumulative effect was made possible by the fact that in the original study the date when the

TABLE 4.—*Heights in Relation to Years in California: Boys* *

		Born Elsewhere							
		1 to 5 Years in California		6 to 10 Years in California		11 Years and Over in California		Number of Children Born in California	Number of Children Born Elsewhere
Age	Born in California Height	Height and Number	Deviation†	Height and Number	Deviation	Height and Number	Deviation		
6	46.04	45.95 465	—0.09	.....	.....	.....	.....	3163	465
7	48.26	48.13 742	—0.13	.....	.....	.....	.....	3409	742
8	50.50	50.15 777	—0.35	50.39 240	—0.11	.....	.....	3475	1017
9	52.60	52.31 808	—0.29	52.50 386	—0.10	.....	.....	3447	1194
10	54.60	54.00 814	—0.60	54.51 516	—0.09	.....	.....	3548	1330
11	56.54	55.82 831	—0.72	56.13 753	—0.41	.....	.....	3819	1584
12	58.54	57.88 762	—0.66	58.06 913	—0.48			3788	1675
13	60.80	60.21 777	—0.59	60.35 906	—0.45	60.78 411	—0.02	3207	2094
14	63.45	63.02 628	—0.43	62.79 886	—0.66	63.36 635	—0.09	2761	2149
15	65.70	64.99 641	—0.71	65.51 913	—0.19	65.44 942	—0.26	2442	2496
16	67.63	66.75 588	—0.88	66.88 780	—0.75	67.12 968	—0.51	1856	2326
17	68.45	67.70 395	—0.75	67.92 546	—0.53	68.03 921	—0.42	1336	1862
18	69.03	68.16 205	—0.87	68.41 278	—0.62	68.38 525	—0.65	599	1008

* All heights and deviations are given in inches.
† Deviation from measurement of children born in California.

child came to California was recorded. This made possible the arrangement of all children of each age into several groups, according to the number of years they had lived in California. One age being dealt with at a time, the weight and height of each child were set down in his appropriate column representing years in California, and the average height and weight figures of each column for years in California were derived. No child was included in this study who had dwelt in California for less than one year. After the exclusion of such children there were available for this study 20,015 white girls and 19,942 white boys who were born outside the state and whose age at entrance to the

state was known.[7] The figures derived thus, representing the heights of the children grouped according to single years of residence in California, are bulky and because of lack of space are not published here. Moreover, though they do show a perceptible upward trend year by year as the time of residence in California increases, there are many deviations from a straight progression upward.

TABLE 5.—*Heights in Relation to Years in California: Girls* *

		Born Elsewhere							
		1 to 5 Years in California		6 to 10 Years in California		11 Years and Over in California		Number of Children Born in California	Number of Children Born Elsewhere
Age	Born in California Height	Height and Number	Deviation†	Height and Number	Deviation	Height and Number	Deviation		
6	45.70	45.54 505	—0.16	.....	.....	.....	.....	2997	505
7	48.02	47.70 647	—0.32	.....	.....	.....	.....	3266	847
8	50.26	49.88 735	—0.38	50.17 203	—0.09	.....	.....	3386	938
9	52.32	51.81 790	—0.51	52.49 350	+0.17	.....	.....	3472	1140
10	54.53	54.05 755	—0.48	53.86 579	—0.67	.....	.....	3481	1334
11	56.71	56.36 804	—0.35	56.61 815	—0.10	.....	.....	3613	1619
12	59.35	58.77 729	—0.58	58.71 797	—0.64	.....	.....	3503	1526
13	61.44	60.75 699	—0.69	60.99 859	—0.45	61.30 426	—0.14	3096	1984
14	62.75	62.44 634	—0.31	62.54 746	—0.21	62.67 714	—0.08	2672	2094
15	63.56	62.90 658	—0.66	63.22 836	—0.34	63.30 929	—0.26	2286	2423
16	63.90	63.08 588	—0.82	63.29 835	—0.61	63.60 1227	—0.30	2111	2650
17	63.99	63.55 445	—0.44	63.56 573	—0.43	63.75 1029	—0.24	1435	2047
18	63.94	63.56 217	—0.38	63.35 292	—0.59	63.80 599	—0.14	608	1108

* All heights and deviations are given in inches.
† Deviation from measurement of children born in California.

To give more graphic accent to this evident trend, the groups of children born elsewhere divided according to single years were merged into five year groups, the thought being that an influence which produces barely perceptible results when operating during a single year might when operating continuously for five years show a clearcut and definite effect. When that merge was made, there was revealed a symmetric upward trend (tables 4 and 5). As a basis for comparison the values

7. The total of the children born elsewhere (39,967) used in the table recording this study differs from the number (40,038) used in table 3 because of exclusion from the present table of all children who had lived in the state of California less than one year.

for the children born in California were used. The differences are shown as deviations (in inches) from the figures for the native-born children of that age. The numbers of children are shown (in bold face type) as evidence that even with this multiple division of the data there are still respectable and significant frequencies from which to derive each value. In tables 4 and 5, 30 values for children born elsewhere are shown, with the deviations; in every case (except 1, in the group of 9 year old girls who had lived six to ten years in California) the deviations are minus—that is, the groups born elsewhere are shorter than the children of the same ages born in California. In effect this is merely a refinement of the conclusions already derived from the comparison of Los Angeles children born in California with Los Angeles children born elsewhere; it demonstrates the consistency with which groups born elsewhere are inferior in stature to the children born in California.

Incidentally, the last two columns give an interesting side light on the magnitude of immigration into California. Among the school children 15 years of age and older, over one-half were born outside the state, and of those 18 years old almost 61 per cent were born outside the state.

Lastly—and this might be considered the most crucial test of the hyphothesis that there is in California a stimulus to extra growth—comparison was made of the deviations among the groups of the same age who were born elsewhere. First, the figure for the two extreme groups were noted, namely those in California one to five years and those in California eleven years and over. This could be done only with children over 13 years of age. Twelve such comparisons were possible (6 for the boys and 6 for the girls), and in each case the children who had been in California the longer time were unmistakably the taller. When the groups who had lived in California one to five years were compared with those who had lived there six to ten years, and when the groups who had lived there six to ten years were compared with those who had lived there eleven years and over, the same relationships were for the most part observed. There seem to be no rational explanations for the fortuitous discrepancies revealed by these comparisons.

No formal measurement of the statistical significance of these deviations was made. In this connection a circumstance of the work is worth mentioning. The data collected in 1936 (76,915 children) were worked up completely during that summer. The data collected in 1936-1937 (35,578 children) were worked up separately in the spring of 1938. The children observed in these two independent but parallel studies were similar, but they were different children from different schools. A comparison of these two series gave a good criterion of the constancy and significance of the findings. It developed that the final figures in the

two series agree so closely that either study could be used by itself as the basis of this paper. It is felt that the ample size of the samples, the consistency and symmetry of the data and the manner in which the separate bits of evidence support each other are adequate evidence that these figures do represent fundamental biologic changes which are the result of California environment.

COMMENT

In the attempt to account for the superiority in height of the Los Angeles children, "California environment" has been repeatedly named as an important cause. Some obvious components of this environment which might be considered unique are increased sunshine, greater variety in diet, more fresh vegetables and fruits and more hours of outside play, all stemming from the more equable climate prevailing in California.

In regard to this so-called "California environment" it is interesting to consider again the comparison of the children of San Francisco with the children of all sections of the United States (tables 1 and 2). Both these groups of children were measured in 1923; in height they are virtually equal. In fact those grouped as children of all sections of the United States have a slight advantage over those of San Francisco. What, then, has become of the influence of California environment in this case? It has apparently failed to operate in San Francisco. Must the basis of the hypothesis be narrowed to include only the influence of *Southern California* environment as providing stimuli to extra growth? Unfortunately the data in this study do not permit the arrangement and comparison of the children on that basis. In contrasting Los Angeles with San Francisco one may be prone to think of the mist and fog characteristic of the bay district as a possible depressing influence on growth. At the same time it must be remembered that the lands of the tallest white men, Scandinavia and the British Isles,[8] are also lands of chill, mist and fog. However, this throws little immediate light on the matter, as racial differences are involved.

In this study a critical attitude has been preserved toward the idea that the growth behavior of Los Angeles children is unique, and any other possible explanation of the findings has been sought. Racial composition has been considered, but test studies on that point have given no grounds for differentiating the white population of Los Angeles (to which race this study is confined) from that of other large cities either in the Central or in the Eastern states. One factor which may possibly be concerned was suggested through a study of the work of Davenport and Love [9] on the United States Army draft for the World War. They

8. Bean, R. B.: Stature Throughout the World, Science **67**:1, 1928.

9. Davenport, C. B., and Love, A. G.: The Medical Department of the United States Army in the World War, Washington, D. C., Government Printing Office, 1921, vol. 15, pt. 1.

compared the average height of the recruits with that of the returning veterans; the latter were 0.23 inch (0.58 cm.) the taller. Davenport and Love suggested that a major factor in causing this difference is the "straightening up" effect of the army drills, of the setting-up exercises and of the army ideals of posture. Los Angeles schools have always laid great emphasis on physical education, but it is especially in the field of correct physical education with its thorough-going postural work as developed by Dr. Sven Lokrantz that Los Angeles schools are outstanding. Is the superior rating of Los Angeles children due in part to the stressing of this postural training in the schools? In securing the present data the workers were specifically coached to give some such command as "Stand tall! Stand erect! Be a soldier!" just as the measurement of height was made. This is common practice in the measuring of children, but possibly the workers in this series carried it out with greater regularity than did the workers in other studies.

In this connection let me again call attention to the fact that every comparison which has been made between Los Angeles children and others in regard to stature has also been made in regard to weight. A whole series of tables comparable to those here presented but showing weights instead of heights has been worked up in manuscript. Body weights are obviously uninfluenced by training in posture or by methods of measurement, yet in these weight tables the position of the Los Angeles children is the same as in the tables in which height is the basis of comparison. Finally, the internal evidence as discussed in this paper in the section on the comparison of Los Angeles children born in California with Los Angeles children born elsewhere and in the section on the comparison among the children born elsewhere, is free from criticism on all these accounts. The data seem capable of only one interpretation, namely, that the superiority in height revealed among the Los Angeles children must in part be put down to environmental influences in that area.

HEMATOLOGIC VALUES FOR NORMAL CHILDREN THREE, FOUR AND FIVE YEARS OF AGE LIVING IN HAWAII

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Studies of the number of erythrocytes and of the quantity of hemoglobin in the blood of normal adults have been numerous during the past two decades. Fewer studies on normal values for these elements in infants and children have been reported, and still less work has been accomplished on the normal values for other blood elements. Previous studies of the blood values of specific age groups have been made as parts of extensive work on blood values for the period of infancy and childhood. In many instances only a small number of children have been studied, and in practically all the studies only a few of the blood elements have been investigated. To a great extent the blood values ascribed to early childhood have been so ascribed by inference from the more thorough studies of the values for the newborn and for infants. It is the purpose of this paper to present the results of a complete hematologic study of healthy children of preschool age (3, 4 and 5 years) residing in the Hawaiian Islands and thereby to contribute to the knowledge of blood values for normal children.

Many of the reports of the earlier investigations of the blood values for infants and children have not been available for use in this study, but reviews of the literature on the hemoglobin levels for the newborn, for infants and for children have been made by Mackay and Goodfellow,[1]

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1. Mackay, H. M. M., and Goodfellow, L.: Nutritional Anemia in Infancy with Special Reference to Iron Deficiency, Medical Research Council, Special Report Series, no. 157, London, His Majesty's Stationery Office, 1931.

Wollstein,[2] Merritt and Davidson,[3] Mugrage and Andresen,[4] Kato and Emery [5] and Faergeman.[6] Of those authors, Merritt and Davidson, Mugrage and Andresen, and Wollstein and Faergemann, and in addition to them, Lippman,[7] have reviewed the literature on the red blood cell values for infants and children. The volume of packed red blood cells, and as a result the corpuscular constants, have not received much consideration except in a few of the more recent investigations. The studies on the values for blood platelets in infants and children have been summarized by Wollstein,[2] McLean, Caffey, Kreidel, Burkland and Brod [8] and Merritt and Davidson.[3] The values for the total number of leukocytes in the blood of infants and children which have been presented in the literature have been summarized by Wollstein,[2] Kato,[9] Washburn,[10] Garrey and Bryan [11] and Magnusson,[12] the last-named author having given particular attention to the total and differential leukocyte counts of young infants.

Studied according to the data reviewed by these authors and to the original data presented by them and other recent investigators,[13] the

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2. Wollstein, M.: The Normal Blood in Infants and Children, in Downey, H.: Handbook of Hematology, New York, Paul B. Hoeber, Inc., 1938, vol. 2.

3. Merritt, K. K., and Davidson, L. T.: The Blood During the First Year of Life, Am. J. Dis. Child. **46**:990 (Nov.) 1933.

4. Mugrage, E. R., and Andresen, M. I.: Values for the Red Blood Cells of Average Infants and Children, Am. J. Dis. Child. **51**:775 (April) 1936.

5. Kato, K., and Emery, O. J.: Hemoglobin Content of the Blood in Infancy, Folia haemat. **49**:106, 1933.

6. Faergeman, P.: The Normal Values for Hemoglobin, Erythrocytes and Cell Volume Per Cent, and the Corpuscular Constants Derived Thereof, in Children Aged Eight to Fourteen Years: Examinations of Three Hundred School-Children in Stockholm, Acta med. Scandinav. **95**:566, 1938.

7. Lippman, H. S.: A Morphologic and Quantitative Study of the Blood Corpuscles in the New-Born Period, Am. J. Dis. Child. **27**:473 (May) 1924.

8. McLean, S.; Caffey, J. P.; Kreidel, K. V.; Burkland, R., and Brod, M.: Blood Platelet Counts in Infants and Young Children, Am. J. Dis. Child. **30**:810 (Dec.) 1935.

9. Kato, K.: Leucocytes in Infancy and Childhood, J. Pediat. **7**:7, 1930.

10. Washburn, A. H.: Blood Cells in Healthy Young Infants: I. The Leukocytic Picture During the First Three Months with Special Reference to Hourly and Daily Variations, Am. J. Dis. Child. **47**:945 (May) 1934.

11. Garrey, W. E., and Bryan, W. R.: Variations in White Blood Cell Counts, Physiol. Rev. **15**:597 (Oct.) 1935.

12. Magnusson, J. H.: On the White Blood Cell Picture During the First Year of Life, Especially with Regard to Its Course, Acta pædiat. **23**:14, 1938.

13. (*a*) Williamson, C. S.: Influence of Age and Sex on Hemoglobin, Arch. Int. Med. **18**:505 (Oct.) 1916. (*b*) Andersen, B., and Ortmann, G.: On the Number of Erythrocytes and the Content of Haemoglobin in the Blood of New-Born Children, Acta med. Scandinav. **93**:410, 1937. (*c*) Rosenbloom, D.: Platelet and Blood Cell Counts in Newborn During First Two Days of Life, Proc. Soc.

(Footnote continued on next page)

levels of some of the blood elements of young children appear to differ markedly from those of adults or of infants, while the levels of other elements seem to differ less decidedly. The quantity of hemoglobin, number of erythrocytes, volume of packed red blood cells, mean corpuscular volume and mean corpuscular hemoglobin are lower for young children than for adults or for the newborn. However, these values are somewhat higher than those for infants, as the lowest normal values for any period occur in early infancy, after a rapid decline from the high values at birth and before a slow increase to adult levels some time during later childhood or adolescence. The values for mean corpuscular hemoglobin concentration appear to be fairly constant throughout life. The numbers of platelets at the various periods of life are so variable that definite conclusions regarding them can be drawn only with difficulty. This difficulty is due to the lack of a standard technic for the enumeration of these elements, but it appears that the number of platelets in children is similar to that in adults. The total white blood cell counts are higher for young children than for adults and lower than for the newborn, childhood and infancy being the period when the white cells decrease from the high levels present at birth to the levels characteristic of adults. The differential leukocyte count for young children is characterized by a lower neutrophil count and a higher lymphocyte count than is the leukocyte count either for adults or for the newborn. The change from the high proportion of neutrophils to the high proportion of lymphocytes of early childhood has been found to occur during early infancy. The reverse change, to the high neutrophil and low lymphocyte

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Exper. Biol. & Med. **32**:906, 1935. (*d*) Lucas, W. P.; Dearing, B. F.; Hoobler, H. R.; Cox, A.; Jones, M. R., and Smyth, F. S.: Blood Studies in the New-Born, Am. J. Dis. Child. **22**:525 (Dec.) 1921. (*e*) Munday, B.; Shepherd, M. L.; Emerson, L.; Hamil, B. M.; Poole, M. W.; Macy, I. G., and Raiford, T. E.: Hemoglobin Differences in Healthy White and Negro Infants, ibid. **55**:776 (April) 1938. (*f*) Sachs, A.; Levine, V. E., and Griffith, W. O.: Copper and Iron in Human Blood: IV. Normal Adolescent Children from Fourteen to Nineteen Years of Age, Arch. Int. Med. **60**:982 (Dec.) 1937. (*g*) Andresen, M. I., and Mugrage, E. R.: Diameter and Volume of Red Blood Cells in Infants and Small Children, Folia haemat. **61**:201, 1938. (*h*) Sanford, H. N.: Effect of Ultraviolet Light on the Blood of the New-Born Infant: Preliminary Reports, Bleeding Time, Coagulation Time and Blood Platelets, Am. J. Dis. Child. **33**:50 (Jan.) 1927; The Effect of Ultraviolet Light on the Blood of New-Born Infants: III. The White Cells, ibid. **37**:1187 (June) 1929. (*i*) Washburn, A. H.: Blood Cells in Healthy Young Infants: II. A Comparison of Routine and Special Technics in the Differentiation of Leukocytes, ibid. **50**:395 (Aug.) 1935; III. A Study of Six Hundred and Eight Differential Leukocyte Counts, with a Final Report of Nine Hundred and Eight Total Leukocyte Counts, ibid. **50**:413 (Aug.) 1935.

TABLE 1.—*Mean Values for Hemoglobin, Erythrocytes and Cell Volume and for Corpuscular Constants for Young Children*

Observer	Place of Study	Number of Subjects*	Age	Method of Hemoglobin Determination	Hemoglobin, Gm. per 100 Cc. of Blood	Erythrocytes, Millions per Cu. Mm. of Blood	Packed Red Cell Volume, Per Cent	Mean Corpuscular Volume, Cubic Microns	Mean Corpuscular Hemoglobin, Micromicrograms	Mean Corpuscular Hemoglobin Concentration, Per Cent
Wollstein [2]	New York	..	2 to 5 yr.	Sahli	14.2	4.39	.....	....	....	....
			5 to 9 yr.		14.6	4.42	.....	....	....	....
Guest, Brown, Wing [17]	Cincinnati	173	2¼ to 3¼ yr.	Palmer	12.4	4.7	.....	78.0	26.5	33.8
		105	3¾ to 5¼ yr.		12.8	4.6	.....	80.0	27.4	34.1
Goldhamer [18]	Ann Arbor, Mich.	31	3 yr.	.....	13.16	....	.....	....	....	....
		31	4 yr.		13.62	....	.....	....	....	....
		35	5 yr.		13.54	....	.....	....	....	....
Mugrage and Andresen [4]	Denver	26	3 to 4 yr.	Van Slyke-Neill oxygen capacity	13.81	4.44	39.61	89.2	29.6	33.2
		23	4 to 5 yr.		13.43	4.43	40.10	90.5	30.3	33.4
		34	5 to 6 yr.		13.27	4.40	39.93	90.7	30.1	33.2
Osgood and Baker [21]	Portland, Ore.	21	4 yr.	Osgood-Haskins	11.65	4.85	34.21†	....	....	....
		21	5 yr.		11.44	4.88	34.40†	....	....	....
Osgood, E. E.; Baker, R. L., and Wilhelm, M. M.: Am. J. Clin. Path. **4**:292 (May) 1934	Portland, Ore.	20	4 yr.	.....	....	4.89	.....	....	....	....
		22	5 yr.		....	4.89	.....	....	....	....
Sobel, I. P., and Drekter, I. J.: Am. J. Dis. Child. **45**:486 (March) 1933	New York	3	3 yr.	Blood iron	12.4	4.58	.....	....	....	....
		5	4 yr.		13.1	5.01	.....	....	....	....
		2	5 yr.		13.4	4.77	.....	....	....	....
Mayers, L. H.: Arch. Int. Med. **30**:478 (Oct.) 1922	Chicago	10	2 yr.	.....	....	5.75	.....	....	....	....
		10	5 to 10 yr.		....	5.21	.....	....	....	....
Mugrage and Andresen [19b]	Denver	..	3 to 8 yr.	Van Slyke-Neill oxygen capacity	13.5	4.40	40.0	....	....	....
Elvehjem and others [16]	Madison, Wis.	..	128 to 152 wk.	Newcomer	12 3	....	.....	....	....	....
			152 to 260 wk.		12.5	....	.....	....	....	....
Osgood [20]	Portland, Ore.	215	4 to 13 yr.	Osgood-Haskins	11.92	5.04	36.0	....	....	....
Andresen, M. I., and Mugrage, E. R.: Am. J. Clin. Path. **8**:46 (Jan.) 1938	Denver	30	2 to 14 yr.	Hellige	13.65	4.59	39.34	85.5	....	....
Faergeman [6]	Stockholm, Sweden	214	8 to 14 yr.	Hellige	13.43	4.73	40.78	86.69	28.5	33.0
Hamre and Wong (Present Study)	Honolulu, Territory of Hawaii	26	3 yr.	.....	14.2	4.98	40.8	83.3	29.3	35.2
		51	4 yr.		13.8	4.80	40.6	84.9	29.1	34.3
		102	5 yr.		13.3	4.79	40.4	85.0	27.9	33.2
		179	3 to 6 yr.		13.6	4.81	40.5	84.7	28.5	33.8

* The subjects included both boys and girls.
† The figures have not been corrected for shrinkage by the anticoagulant.

values of the adult, appears to be a slow change which continues throughout most of childhood.

Though the values reported for the various blood elements of childhood are not in absolute agreement, the greater number tend to support the view that the changes follow a definite developmental course. The blood values which have been reported for early childhood or for the entire period of childhood are summarized in tables 1 and 2.

SUBJECTS

All of the children whose blood was examined in this study were residents of Honolulu, and none of them had resided elsewhere than in the Hawaiian Islands for the year and a half before the hematologic examinations. Most of the subjects were born in Honolulu.

Eighty-nine girls and 90 boys were studied. They ranged in age from 3 years, 6 days to 5 years, 338 days, thus comprising an age group of from 3 to 6 years. The children had all been examined by physicians and dentists previous to the blood examinations and were considered to be in average good health. Ten girls and 8 boys were found to be infected with pinworms (Enterobius vermicularis), but since on reexamination after treatment for the parasites the blood showed no changes, the first values for these children, which were similar to those for nonparasitized children, were included in the final data.

The economic and social status of the children's parents varied. None of the children, however, were from poor families and none were from wealthy families; instead, they were from families of average means. The children also differed racially.

The numbers of subjects considered in respect to each race, age and sex are summarized in tables 3 and 4. In view of their health, their race and the economic status of their parents, we feel that the subjects represent a cross section of the average healthy children of Honolulu.

METHODS

The blood samples were peripheral blood obtained from the lobe of the ear by puncture with a spring lancet. Twenty-five of the hemoglobin determinations were made by the Newcomer method, with a Bausch and Lomb colorimeter equipped with a standard color disk. The remaining one hundred and fifty-four hemoglobin determinations were made by the acid hematin method, with a Summerson test tube photoelectric colorimeter manufactured by the Klett Manufacturing Company. The colorimeter was standardized against Van Slyke's oxygen capacity method of hemoglobin determination.

Blood samples for the enumeration of erythrocytes, platelets and leukocytes were taken with Thoma pipets, and Hayem's and Türk's solution and the solution of Reese and Ecker were used as diluents. All enumerations were made by the direct method, with the use of Levy counting chambers with double Neubauer ruling. All pipets and counting chambers were certified for accuracy by the United States Bureau of Standards. The volume of packed red blood cells were determined on peripheral blood collected in capillary pipets and centrifuged at 3,200 revolutions per minute for thirty minutes or longer, according to the method described else-

TABLE 2.—*Mean Values for Platelet, Leukocyte and Differential Leukocyte Counts for Young Children*

Observer	Place of Study	Number of Subjects*	Age in Years	Platelets per Cu. Mm. of Blood	Leukocytes per Cu. Mm. of Blood	Differential Leukocyte Count, Per Cent					
						Neutrophils	"Stab" Cells	Eosinophils	Basophils	Lymphocytes	Monocytes
Osgood [20]	Portland, Ore.	219	4 to 13	.....	.....	....	3.07	2.79	...	....	3.08
		86	4 to 7	.....	10,365	....	...	...	...	....	...
		597	4 to 30	.....	.....	....	...	...	0.52	....	...
		242	8 to 18	.....	8,342	....	...	...	...	....	...
		241	4 to 14	.....	.....	37.60	...	...	...	48.21	...
		120	15 to 19	.....	.....	47.65	...	...	...	41.91	...
Wollstein [2]	New York	...	2 to 5	.....	8,915	45.0	...	2.0	0.0	50.0	3.0
		...	5 to 9	.....	7,386	53.0	...	2.0	1.0	41.0	3.0
		...	9 to 12	.....	6,425	68.0	...	1.0	0.0	29.0	2.0
Benjamin, B., and Ward, S. M.: Am. J. Dis. Child. 44: 921 (Nov.) 1932	New York	...	2 to 3	.....	9,400	50.0	...	2.7	0.5	39.4	7.4
		...	3 to 4	.....	8,900	52.8	...	2.8	0.4	36.0	7.9
		...	4 to 5	.....	8,900	55.1	...	2.8	0.4	32.6	9.0
		...	5 to 6	.....	8,900	57.3	...	2.8	0.4	30.3	9.0
McLean, Caffey and others [5]	New York	2	3	260,000	12,575	....	...	...	...	....	...
		1	3½	264,000	22,400	....	...	...	...	....	...
		1	4½	368,000	12,200	....	...	...	...	....	...
		1	6½	280,000	6,800	....	...	...	...	....	...
Goldhamer [18]	Ann Arbor, Mich.	150	2 to 3	.....	7,350	48.2	...	3.9	...	38.4	4.5
		150	3 to 4	.....	6,400	52.6	...	5.7	...	33.2	4.2
		150	4 to 5	.....	6,560	61.0	...	6.3	...	25.8	3.7
Osgood, E. E.; Baker, R. L.; Brownlee, I. E.; Osgood, M. W.; Ellis, D. M., and Cohen, W.: Am. J. Dis. Child. 58: 61 (July) 1939	Portland, Ore.	22	4	.....	10,440	36.00	3.7	2.8	0.9	47.8	3.1
		21	5	.....	9,720	36.4	3.5	2.8	0.5	47.8	3.5
		22	6	.....	11,200	37.10	2.3	2.2	0.5	51.6	2.9
		21	7	.....	10,100	39.8	2.2	3.2	0.7	48.5	2.7
		86	4 to 7	.....	10,370	37.30	2.6	2.7	0.7	48.9	3.0
Hanson and Wong (Present Study)	Honolulu, Territory of Hawaii	26	3	272,000	8,158	33.6	6.2	3.6	0.3	51.9	4.3
		51	4	269,000	8,020	37.7	4.4	5.3	0.4	47.2	5.0
		102	5	315,000	7,770	39.6	2.7	5.0	0.3	48.2	4.2
		179	3 to 6	295,000	7,900	38.2	3.7	4.9	0.3	48.4	4.5

* The subjects included both boys and girls.

where by one of us.[14] The formulas proposed by Wintrobe [15] were used in calculating the corpuscular constants.

Blood smears for the differential leukocyte counts were made by the usual technic and stained with Wright's stain. One hundred cells from three different slides were counted for each child, and the average was taken as the differential count for the child.

RESULTS

The data obtained in this investigation were studied with the purpose of determining, if possible, whether differences in respect to sex, age or race might occur in the values for the various blood elements. It was decided that if no such differences were observed, the values for all children studied would be combined and the data would be treated statistically with the aim of establishing mean values and statistical constants for the blood elements of normal children 3 to 6 years of age.

Racial Differences.—The average values for the various blood elements of the different racial groups studied are presented in table 3. Statistical constants and critical ratios are omitted because statistically significant differences did not occur.

Age and Sex Differences.—The average values for the blood elements of boys and girls of different ages are presented in table 4. Slight differences are exhibited for several of the blood elements for the different ages. In all instances statistical analysis showed that these differences were not significant. It is doubtful whether the slight differences observed indicated a tendency toward an increase or decrease with age. The only blood element of which the critical ratio approached significance was the "stab" cells of the differential count. In this element the tendency toward a decrease with age is indicated. Coincident with this decrease, a proportionate increase in the mature type of neutrophil cells would be expected. This increase is not clearly evident from the average values obtained, and the statistical analysis does not indicate it. In general, it can be concluded that for the age group of 3 to 6 years, one of narrow span, significant differences with age do not occur for any of the blood elements observed.

Sexual differences indicated for the average blood values of the children in this study were slight and statistically not significant.

Hematologic Values for the Entire Group.—Since no differences in respect to race, sex or age were observed in the values for the various hematologic elements, it was possible to combine the values for all children for the purpose of determining normal hematologic values for this

14. Hamre, C. J.: The Capillary Hematocrit Method of Determining Blood Cell Volume, J. Lab. & Clin. Med. **25**:547 (Feb.) 1940.

15. Wintrobe, M. M.: The Size and Hemoglobin Content of Erythrocytes: Methods of Determination and Clinical Application, J. Lab. & Clin. Med. **17**:899 (June) 1932.

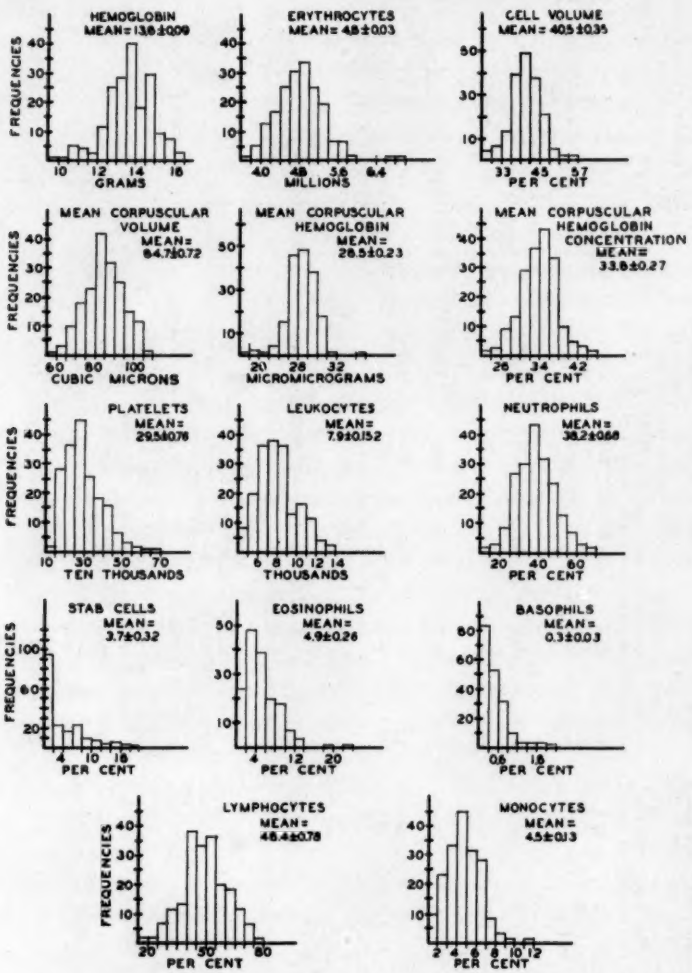
TABLE 3.—*Comparison of Mean Blood Values of Different Races*

Race	Number of Subjects	Average Hemoglobin, Grams per 100 Cc. of Blood	Average Number of Erythrocytes, Millions per Cu. Mm. of Blood	Average Volume of Packed Red Cells, Cc. per 100 Cc. of Blood	Mean Corpuscular Volume, Cubic Microns	Mean Corpuscular Hemoglobin, Micromicrograms	Mean Corpuscular Hemoglobin Concentration, per Cent	Average Number of Platelets, Thousands per Cu. Mm. of Blood	Average Number of Leukocytes per Cu. Mm. of Blood	Average Differential Leukocyte Count, Per Cent					
										Neutrophils	"Stab" Cells	Eosinophils	Basophils	Lymphocytes	Monocytes
Caucasian.....	33	13.9	4.74	41.5	87.7	29.4	33.8	292	8,040	35.5	2.5	4.0	0.4	52.7	5.0
Chinese.....	33	13.7	4.91	40.0	82.3	28.4	34 5	303	8,310	39.7	4.8	5.0	0.3	45.8	4.4
Japanese.....	50	13.8	4.81	41.5	86.6	28.9	33.5	279	7,870	38.8	3.8	4.9	0.4	47.5	4.8
Korean.....	6	13.5	4.75	41.4	87.5	28.8	32.8	297	7,710	44.5	2.5	4.2	0.5	44.3	3.9
Caucasian-Hawaiian.....	22	13.3	4.77	38.3	81.0	28.1	34.7	300	7,490	37.0	4.4	5.3	0.3	48.8	4.3
Caucasian-Oriental.....	6	13.3	5.01	42.4	84.7	26.6	31.7	345	8,150	38.7	2.9	5.2	0.3	48.5	4.4
Caucasian-Oriental-Hawaiian.....	7	13.0	4.71	39.0	83.3	27.7	33.6	292	6,520	37.8	2.7	4.8	0.4	50.3	4.0
Oriental-Hawaiian.....	11	12.9	4.78	39.5	83.2	27.1	33.1	330	7,370	40.2	3.0	6.8	0.1	46.1	3.8
All others.....	11	13.1	4.82	40.0	82.9	27.1	32.9	289	8,430	35.9	4.4	5.5	0.1	50.5	3.5

TABLE 4.—*Comparison of Mean Blood Values in Respect to Sex and Age*

Age Group in Years	Sex	Number of Subjects	Average Hemoglobin, Grams per 100 Cc. of Blood	Average Number of Erythrocytes Millions per Cu. Mm. of Blood	Average Volume of Packed Red Cells, Cc. per 100 Cc. of Blood	Mean Corpuscular Volume, Cubic Microns	Mean Corpuscular Hemoglobin, Micromicrograms	Mean Corpuscular Hemoglobin Concentration, per Cent	Average Number of Platelets, Thousands per Cu. Mm. of Blood	Average Number of Leukocytes per Cu. Mm. of Blood	Average Differential Leukocyte Count, per Cent					
											Neutrophils	"Stab" Cells	Eosinophils	Basophils	Lymphocytes	Monocytes
3	M	13	14.2	4.82	40.4	83.9	29.6	35.3	277	8,580	33.9	5.8	4.9	0.4	50.6	4.4
	F	13	14.3	5.03	41.2	82.6	29.0	35.2	267	7,780	33.3	6.6	2.3	0.3	53.2	4.3
	M and F	26	14.2	4.93	40.8	83.3	29.3	35.2	272	8,158	33.6	6.2	3.6	0.3	51.9	4.3
4	M	24	13.8	4.77	39.8	84.0	29.0	34.8	274	7,810	37.4	4.3	6.0	0.4	46.5	5.4
	F	27	13.9	4.83	41.3	85.7	29.1	33.8	264	8,210	38.0	4.5	4.8	0.3	47.8	4.7
	M and F	51	13.8	4.80	40.6	84.9	29.1	34.3	269	8,020	37.7	4.4	5.3	0.4	47.2	5.0
5	M	53	13.2	4.77	39.8	84.0	27.8	33.5	314	7,980	39.8	3.5	5.2	0.3	46.7	4.6
	F	49	13.4	4.81	41.2	86.1	28.1	32.8	316	7,570	39.3	1.8	4.9	0.3	49.8	3 9
	M and F	102	13.3	4.79	40.4	85.0	27.9	33.2	315	7,770	39.6	2.7	5.0	0.3	48.2	4.2
3-4-5	M	90	13.5	4.77	39.9	84.0	28.4	34.1	298	8,010	38.3	4.0	5.3	0.4	47.2	4.8
	F	89	13.7	4.85	41.2	85.5	28.5	33.5	293	7,790	38.0	3.3	4.5	0.3	49.7	4.2
	M and F	179	13.6	4.81	40.5	84.7	28.5	33.8	295	7,900	38.2	3.7	4.9	0.3	48.4	4.5

age group. Table 5 contains the mean values for all blood elements and the statistical constants for these values as well as the range of the values observed. The frequencies of occurrence of the different values for the various blood elements are graphically presented in the accompanying histograms.



Frequency distribution of various blood values.

Additional Observations.—The highest hematologic values encountered in this study were observed in the blood of 3 children who were considered to be overweight according to the Emerson table of normal height and weight measurements adopted by the Territorial Department of Public Instruction. We were thus led to investigate the probable effect of body weight on blood values, but found that the number of

cases available was insufficient to permit statistically positive conclusions. However, there were in the series 10 children who were 5 pounds (2.25 Kg.) or more overweight and 10 who were 5 pounds or more

TABLE 5.—*Mean Values, Statistical Constants and Range of Values for Entire Study*

Blood Element	Mean Value	Standard Error of the Mean	Standard Deviation	Standard Error of the Standard Deviation	Range
Hemoglobin, grams per 100 cc. of blood	13.6	0.090	1.20	0.063	9.8 to 16.1
Erythrocytes, millions per cu. mm. of blood	4.81	0.037	0.50	0.026	3.80 to 6.83
Volume of packed red blood cells, cc. per 100 cc. of blood	40.5	0.347	4.64	0.245	28.6 to 55.6
Mean corpuscular hemoglobin, micromicrograms	28.5	0.231	3.09	0.163	17.7 to 41.0
Mean corpuscular hemoglobin concentrations, per cent	33.8	0.271	3.62	0.191	23.0 to 44.0
Mean corpuscular volume, cubic microns	84.7	0.720	9.63	0.509	59.0 to 109.4
Platelets, ten thousands per cu. mm. of blood	29.5	0.759	10.15	0.536	13.8 to 68.1
Leukocytes, thousands per cu. mm. of blood	7.90	0.152	2.03	0.107	4.0 to 13.8
Differential leukocyte count, per cent					
Neutrophils	38.2	0.683	9.14	0.483	12.7 to 67.3
"Stab" cells	3.7	0.321	4.30	0.227	0.0 to 18.3
Eosinophils	4.9	0.255	3.41	0.180	0.7 to 22.7
Basophils	0.3	0.028	0.37	0.019	0.0 to 2.3
Lymphocytes	48.4	0.777	10.44	0.550	18.0 to 77.3
Monocytes	4.5	0.131	1.75	0.092	1.7 to 11.7

TABLE 6.—*Mean Values for Entire Group, for Underweight and Overweight Children, for Children of Poor Families and for Children Infested with Pinworms*

Blood Element	Entire Group	Underweight Children (N = 10)*	Overweight Children (N = 10)	Children of Poorer Families (N = 39)	Children Infested with Pinworms (N = 18)
Hemoglobin, grams per 100 cc. of blood	13.6	13.8	13.4	13.3	14.3
Erythrocytes, millions per cu. mm. of blood	4.81	4.64	4.90	4.94	4.54
Volume of packed red blood cells, cc. per 100 cc. of blood	40.5	39.8	39.0	40.6	42.5
Mean corpuscular hemoglobin, micromicrograms	28.5	29.9	27.3	27.2	31.9
Mean corpuscular hemoglobin concentration, per cent	33.8	34.9	34.7	33.1	33.7
Mean corpuscular volume, cubic microns	84.7	86.0	80.2	82.5	93.8
Platelets, ten thousands per cu. mm. of blood	29.5	33.2	37.6	32.5	27.4
Leukocytes, thousands per cu. mm. of blood	7.90	8.29	7.78	8.56	7.73
Differential leukocyte count, per cent					
Neutrophils	38.2	39.1	36.6	41.4	41.6
"Stab" cells	3.7	3.5	2.6	4.2	0.1
Eosinophils	4.9	4.7	4.9	5.2	5.2
Basophils	0.3	0.3	0.4	0.2	0.5
Lymphocytes	48.4	48.0	51.3	44.6	47.8
Monocytes	4.5	4.5	4.1	4.3	4.8

* N represents the number of children.

underweight. The mean values for the two groups compared well with each other and with the mean values for the complete study. The comparative values are presented in table 6.

By a similar method of study we were unable to observe any definite influence of the social and economic position of the parents on the blood

values of the children. Blood values of children from homes with incomes of over $100 per month showed as much variation about the mean values for the entire group as did those of children from families with incomes of under $100 per month. The mean values for the children of the group with low incomes are also presented in table 6.

At the time of our studies the children were being examined by other investigators for information on the occurrence of helminth infections. Eighteen of the children examined were found to be infested with pinworms (Enterobius vermicularis), and consequently observations on the influence of pinworm infections on the blood picture were included in this hematologic study. A comparison of the mean hematologic values of the infected group with the mean values of the entire group failed to show any influence of the infections. The conclusion that there was no such influence was strengthened by the fact that a reexamination of some of the children after treatment for elimination of the parasites revealed that no changes in the blood values had occurred. The mean blood values for the parasitized group of children are included in table 6.

COMMENT

Our conclusion that sex and age are not significant influences on the blood values of children is not a new one. The same conclusion has been drawn by Elvehjem, Peterson and Mendenhall,[16] Faergeman,[6] Guest, Brown and Wing,[17] Goldhamer,[18] Mugrage and Andresen,[19] Osgood,[20] Osgood and Baker [21] and many others. The question of the influence of race on blood values, however, is one on which very little direct work has been undertaken. Munday and others [13e] have reported that they have observed a consistently lower hemoglobin value for Negro infants 3 to 54 weeks of age than for white infants of comparable ages, the differences amounting to 0.5 to 1.0 Gm. of hemoglobin per

16. Elvehjem, C. A.; Peterson, W. H., and Mendenhall, D. R.: Hemoglobin Content of the Blood of Infants, Am. J. Dis. Child. **46**:105 (July) 1933.

17. Guest, G. M.; Brown, E. W., and Wing, M.: Erythrocytes and Hemoglobin of the Blood in Infancy and Childhood, Am. J. Dis. Child. **56**:529 (Sept.) 1938.

18. Goldhamer, S. M.: Special Features of the Blood in Infancy and Childhood, J. Lab. & Clin. Med. **17**:1043 (July) 1932.

19. Mugrage, E. R., and Andresen, M. I.: (*a*) Values for Red Blood Cells of Average Infants and Children, Am. J. Dis. Child. **51**:775 (April) 1936; (*b*) Normal Standards for Red Blood Cell Values in Colorado, Colorado Med. **34**:473 (July) 1937; (*c*) Red Blood Cell Values in Adolescence, Am. J. Dis. Child. **56**: 997 (Nov.) 1938.

20. Osgood, E. E.: Normal Hematologic Standards, Arch. Int. Med. **56**:845 (Nov.) 1935.

21. Osgood, E. E., and Baker, R. L.: Erythrocytes, Hemoglobin, Cell Volume and Color, Volume and Saturation Index Standards for Normal Children of School Age, Am. J. Dis. Child. **50**:343 (Aug.) 1935.

hundred cubic centimeters of blood. However, they were unable to detect significant differences between the red blood cell values for the infants of the two races. Nelson and Stoker,[22] in a study of the hemoglobin and red cell values for men, found no differences between the Negro and white races in respect to these values. It is possible that racial differences may occur for certain periods of life, but it is also possible that such apparent periodic differences may be due to other factors.

Great uniformity in the mean hemoglobin values occurred among the children of the various racial groups whom we studied. Even the 1 Gm. difference occurring between the mean hemoglobin value of 13.9 for Caucasian children and that of 12.9 for Oriental-Hawaiian children was found to be statistically not significant, the critical ratio being 1.36. Because of this observation and because the hemoglobin values in all other instances were more closely similar, we have concluded that racial differences in hemoglobin values do not exist. In this we are in agreement with the opinion expressed by Myers and Eddy,[23] who, after a study of the hemoglobin values obtained by a number of investigators for men and women of various parts of the world, concluded that racial differences in hemoglobin values do not occur. It is important to note that not only hemoglobin values but the values for all the hematologic elements obtained in this study showed no racial differences.

A study of tables 1 and 2, in which blood values for subjects of this specific age group and for children are summarized from the literature, shows that the mean values for all blood elements obtained in this study compare closely with those given by other investigators. It may be concluded that there are no significant differences between the values for hemoglobin, number of red blood cells, volume of packed red blood cells or the corpuscular constants among children residing in the Hawaiian Islands and those among children residing in other parts of the world. The differences between our values for platelets and those of other investigators, shown in table 2, are slight and insignificant when full consideration is given to the large technical error commonly encountered in making platelet counts and to the extreme variability of the number of platelets in normal persons. Our values for white blood cells are in fairly close agreement with those of other investigators, and it is unlikely that the small differences between the values reached in this study and those reported in the literature are due to geographic influences. Our results for the differential leukocyte counts are also in general agree-

22. Nelson, C. F., and Stoker, R.: The Hemoglobin Concentration and Erythrocyte Counts of Healthy Men, Folia haemat. **58**:333, 1937.

23. Myers, V. C., and Eddy, H. M.: The Hemoglobin Content of Human Blood Cells, J. Lab. & Clin. Med. **24**:502 (Feb.) 1939.

ment with those of other workers in that the neutrophil count is low while the lymphocyte count is high for children. It may be concluded that all blood values for normal healthy children of the Hawaiian Islands are similar to those for normal children of the same age residing in other parts of the world and that geographic influences on blood values are negligible.

It has frequently been pointed out that detectable differences occur in the blood values of persons of different types of body build. Osgood and Haskins [24] have indicated that the red blood cell count is higher among thin or muscular persons than among stout persons. In our studies we made careful observations of the possible relations of body weight to blood values. The results of only a small portion of the study are presented in table 6. With the possible exception of the values for the red blood cells, consistently higher or lower values could not be demonstrated for overweight or underweight children. The differences for the number of red blood cells were not statistically significant but were higher for the stout than for the thin, muscular persons. Our observations indicated that among children no type of body build is associated with a particular type of hematologic value.

From the study of the relation of the family income to blood values, which we made in addition to the study of the relation of body build to blood values, we came to the conclusion that for our group of children no relationship between income and blood values existed. The blood values for the children of the low income group compared closely in every respect to those for children of higher income families.

Pinworms are known to be present in children frequently. Their presence, according to Gradwohl,[25] does not often produce symptoms of anemia, or, according to Griffith and Mitchell,[26] does not cause any certain increase in the number of circulating eosinophils. The blood values we obtained for children infested with pinworms were so similar to those for the children not infested that for our group of children we concluded that the parasites had exerted no influence on any element of the blood picture. The highest eosinophil counts observed were in children free of pinworms and other parasites, and the resulting conclusion that pinworm infections of the kind observed in our study do not influence the eosinophil values agrees with that of Griffith and Mitchell.[26]

24. Osgood, E. E., and Haskins, H. D.: A Textbook of Laboratory Diagnosis, Philadelphia, P. Blakiston's Son & Co., 1931.

25. Gradwohl, R. H. B.: Clinical Laboratory Methods and Diagnosis, St. Louis, C. V. Mosby Company, 1935.

26. Griffith, J. P. C., and Mitchell, A. G.: The Diseases of Infants and Children, Philadelphia, W. B. Saunders Company, 1937.

SUMMARY

Data for the hematologic values of 179 healthy children residing in the Hawaiian Islands are presented. The children observed varied in age from 3 to 6 years and were from several different races. No differences in respect to age, sex or race occurred in the values of the various blood elements. The mean blood values compare closely to those given by other investigators for children of other parts of the world, and it is concluded that the blood levels for the children of the Hawaiian Islands do not differ significantly from those for children of other parts of the world. The mean values, the statistical constants and the range of observed values for the various blood elements are summarized (table 5).

EFFECT OF HUMAN SERUM ON THE SCHICK REACTION AND THE BLOOD ANTITOXIN TITER

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In a previous communication [1] we reported the results of a four year study of the routine inoculation with parental serum of every child admitted to the pediatric service. The findings indicated a definite diminution in the incidence of secondary infectious diseases, in contrast to the number which developed in the surgical pediatric ward, which served as a control.

The purpose of the present study was to determine, if possible, the exact nature of the protection which parental serum apparently conferred on its recipients. Because of the fact that susceptibility of a person to diphtheria can be determined within twenty-four hours by means of the Schick reaction, which is accepted as a criterion from the practical point of view, diphtheria was singled out for special study. Moreover, we felt that by studying the effect of human serum in a disease immunity to which can be measured on an accurate and quantitative basis we could gain a better insight into the subject of immunity and its duration.

There has been no lack of investigation of the Schick reaction, covering almost every angle of the problem. Little investigation, however, has been carried out with regard to the effect of human serum on the cutaneous reaction produced by the Schick test. The only reference found in this connection is that of Thelander [2] in 1934. She reported her observation regarding the reversibility of the Schick reaction by means of injection of human blood. Four to 6 cc. of blood was injected intramuscularly in 6 persons with a positive Schick

From the department of Pediatrics, Morrisania City Hospital.

1. Barenberg, L. H.; Greene, D., and Grand, M. J. H.: Prophylactic Use of Parental Blood Serum Against Contagion in a Pediatric Ward, Am. J. Dis. Child. **57**:322 (Feb.) 1939.

2. Thelander, H. E.: Neutralization of the Schick Reaction by Human Blood, J. Pediat. **4**:75 (Jan.) 1934.

reaction, and within twenty-four hours after the injection 4 of the 6 had a negative reaction. Later 1 of the 2 remaining patients received a transfusion, subsequent to which the reaction became negative.

MATERIAL

This investigation was based on a study of 1,498 Schick tests performed on 1,189 patients who were admitted to the pediatric service for the last nineteen months, from December 1937 to June 1939 inclusive. In 426 of the patients, or 35.8 per cent, the cutaneous reaction was positive on admission. In 763, or 64.2 per cent, the reaction was negative. One or more repeated tests were done on 141 persons subsequent to the injection of human serum. On 39, or 3.3 per cent, of the persons the test was done but the patient either left the hospital or died before the Schick reaction could be read. In addition to the studies of the Schick tests titrations of the blood of 55 children were done (table 1). Con-

TABLE 1.—*Summary of Material Studied*

Number of patients admitted (12-19-37 to 6-31-39)	1,189
Number of Schick tests on admission	1,189
Number of retests	309
Total number of Schick tests performed	1,498
Number of positive Schick reactions	426
Percentage of positive Schick reactions	35.8%
Number of patients who left the hospital before the reading of the Schick reactions	39
	3.3%
Number of repeated Schick tests	309
Range of age of children studied	6 mo. to 12 yr.
Number of cases in which serum was titrated	55

currently with this study accurate records were kept concerning the effect of human serum on other cutaneous reactions such as the Dick and the Mantoux. Our observations with regard to the effect of serum on the cutaneous reaction produced by the Dick toxin will be the subject of a future communication.

A Schick test and a control test with heated toxin were done by the resident physician on the anterior surface of the left arm of every patient over 3 months of age. The observations of the cutaneous reaction were carried out by one of us (N.G.); readings were made daily for a period of seven days to eliminate transitional positive Schick reactions. This phenomenon, as Schick pointed out,[3] is found in persons whose serum antitoxin content is insufficient to neutralize completely the toxin in the area into which the injection is made, but enough to check the specific inflammatory reaction after an interval of from twenty-four to forty-eight hours. In the reading of the original and the subsequent Schick reaction, not only were the size and the intensity of the reaction noted, but cognizance was taken of the presence or absence of an area of central pallor or a vesicle in the lesion. The patients with positive Schick reactions were

3. Michiels, J., and Schick, B.: Die Intrakutanreaktion des Menschen auf Diphtherietoxininjection, Ztschr. f. Kinderh. **5**:349, 1912.

given retests, including the control test, within an interval of a few days to two weeks after the injection of serum. If the reaction remained positive no further attempt was made to repeat the test except in a few instances. In the event a reversal took place, the patient was requested to return to our clinic at monthly intervals for a retest. We contended with the difficulties incident to any study which is made partly in an outpatient clinic. In spite of follow-up activities of the social service department, the mothers failed to bring their children at the appointed time, and the retests, therefore, were done at varying intervals.

An intramuscular injection of human serum giving a negative Wassermann reaction was given to every patient within twenty-four hours after admission. At the beginning, serum of a parent or of a guardian was used. This of necessity caused a delay of one or two days in the injection of the serum before the report on the Wassermann reaction was obtained. To expedite the procedure, negatively reacting human serum which we had had on hand was given immediately on admission. The technic of collecting and administering the serum did not differ from that described in a previous report [1] except that during the period of titration studies part of the donors' blood was set aside to be used for determinations of antibody titer. The original dose of the serum employed was about 20 cc. except in patients suffering from pneumonia, for whom the amount used was much greater, and the injection was repeated on three consecutive days. Later it was deemed advisable to increase the serum to 30 cc., an amount equivalent to six times that of measles convalescent serum necessary for measles prophylaxis. During the period of titration studies the amount of serum was gradually reduced in some instances to as low as 10 cc. to enable us to observe the effect of a minimum amount on the response of the titer in the blood and on the Schick reaction. The few changes in the routine introduced during the course of the study did not alter the final results, as will be seen in the subsequent paragraph.

In the investigation we sought to ascertain whether the reversal of a positive Schick reaction by means of injection of human serum indicates increased antitoxin titer of the blood of the recipient. To that end, after the study was well under way for nearly a year, serum titrations were begun on both the donor and the patient; the blood of the latter was titrated before and after the serum was injected. The method employed is that described by Jensen [4] and is the official method used at the laboratories of the New York city health department.

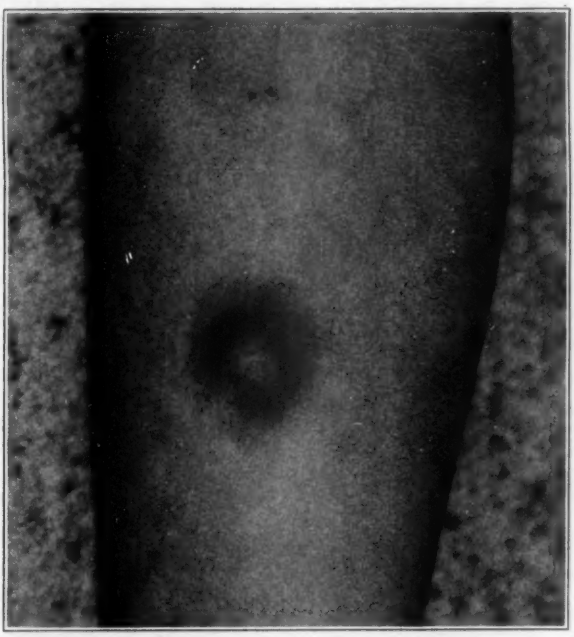
RESULTS

A phenomenon which is interesting and which has not, to our knowledge, been previously described, is the central pallor resulting from the Schick test. It was noted that within twenty-four hours after the injection of the serum a pallor developed in the center of the area of the Schick reaction; the erythema began to fade radially and within forty-eight hours there was a clear demarcation between the central pallor and the peripheral inflammatory zone, as shown in the accompanying photograph. In cases in which serum was not given, the

4. Jensen, C.: Die intrakutane Kaninchenmethode zur Auswertung von Diphtherie-Toxin und Antitoxin, Acta path. et microbiol. Scandinav. 1933, supp. 14, pp. 1-211.

cutaneous lesion produced by the test usually lasted for a week or more, when involution began in the center, while the dark brown pigmentation and scaling persisted in some cases for as long as three to four months. Whether the blanching phenomenon produced by the human serum is analogous to the Schultz-Charlton reaction in scarlet fever, we are unable to say.

In the early period of the study we attempted to predict in advance by the presence of central pallor a reversal of the positive Schick reaction. However, as it will be brought out later, this anomaly had no relationship to the reversibility of the Schick reaction.



Cutaneous reaction to the Schick test, showing an area of central pallor within the peripheral inflammatory zone.

After our studies had been in progress for some time it became apparent that all the cases in which the Schick reaction was positive fell into two groups, namely, those in which the reaction was persistently positive and those in which the cutaneous reaction became negative after the injection of serum.

Cases in Which the Schick Reaction Was Persistently Positive After Injection of Serum.—The data for analysis of this group comprise eighty-six observations of cutaneous reaction on 43 children ranging from 6 months to 12 years of age. In addition, blood titrations were done on 22 of this group of children (table 2).

TABLE 2.—*Summary of Observations on Patients Whose Schick Reaction Remained Persistently Positive After Injection of Serum*

Age Group	Number of Children	Children Immunized Before Admission*	Serum Average (Cc.)	Schick Test Before Serum: Intensity Degree	Schick Test Before Serum: Intensity Number of Cases	Schick Test Before Serum: Central Pallor Present	Schick Test Before Serum: Central Pallor Number of Cases	Schick Test Before Serum: Between Schick Test and Serum, (Average Number Days)	Schick Test After Serum: Intensity Degree	Schick Test After Serum: Intensity Number of Cases	Schick Test After Serum: Central Pallor Present	Schick Test After Serum: Central Pallor Number of Cases	Schick Test After Serum: Between Serum and Second Schick Test, (Average Number Days)	Titration of Serum (Average Units per Cc.†): Donor	Titration of Serum (Average Units per Cc.†): Patient Before Serum	Titration of Serum (Average Units per Cc.†): Patient After Serum	Serum Injection to Second Titration, (Average Number of Days)	Second Schick Test to Second Titration, (Average Number of Days)
6 mo. to 3 yr.	25	4	20.8	+	11	No	20	5.6	+	21	No	23	5.1	0.0187	0.0036	0.0052	6.2	2.2
				++	11	....	..	...	++	4	....	..						
				+++	3	Yes	5	...	+++	0	Yes	2						
3 to 6 yr.	11	1	24.7	+	8	No	9	3.4	+	11	No	8	6.8	0.03	0.0075	0.01	5.0	0.0
				++	2	....	..	...	++	0	....	..						
				+++	1	Yes	2	...	+++	0	Yes	3						
6 to 12 yr.	7	1	24.2	+	3	No	5	5.1	+	7	No	7	5.6	0.0076	0.0036	0.0043	6.0	2.6
				++	4	....	..	...	++	0	....	..						
				+++	0	Yes	2	...	+++	0	Yes	0						

* By 2 or more previous injections of alum or toxoid.

† Blood titrations were done on 17 children of the first age group, 2 of the second and 3 of the third.

There is an essential difference in the susceptibility to diphtheria according to the age of the children. For instance, infants under 6 months still possess some immunity imparted to them by the mother who has a natural or acquired immunity to diphtheria. From this age on there is a gradual but steady decline in the immunity of the children, so that at the end of the second year of life, when the particular blood group has developed in the majority of the children, the amount of antitoxin in their serum is almost at its minimum. The incidence of positive Schick reactions steadily rises up to the age of 5 years. Thereafter the incidence declines. It would seem that age brings with it a certain degree of immunity to diphtheria as to some of the other infectious diseases. It may be that this specific immunity is brought about by the fact that the tissues have to react repeatedly to small exposures to specific infections. It would be a palpable error, therefore, to compare the incidence and the nature of the cutaneous reaction among infants with those of the reaction among older children. We therefore divided the children arbitrarily into three age groups: from 6 months to 3 years; from 3 years to 6 years, and from 6 to 12 years.

A glance at table 2 reveals that 84 per cent of the children were under 6 years of age, in a period in life when children have the least amount of contact with diphtheria toxins except through the prophylactic diphtheria inoculation and are consequently, as we have said, slower in acquiring immunity. In our series even the 5 children who received sufficient toxoid in one form or another did not become immune, as indicated by the persistently positive Schick reaction.

Many workers in this field have stated that there is no correlation between the intensity of the cutaneous reaction and the antitoxin level of the serum. However, when a factor is introduced in the procedure, such as injection of human serum, such an assertion may not hold true. A comparison of the intensity of reaction to the first and the second Schick test reveals that there were 21 moderately severe reactions to the first and only 4 to the retest following injection of human serum. Moreover, in 5 children the original Schick test was associated with vesicle formation, whereas with the retest no such formation occurred. It will be shown subsequently that the decrease in intensity of the Schick reaction was associated with a slight but definite rise in the blood titer.

That the amount of serum alone was not the main factor responsible for the failure to produce a reversal of the Schick reaction became apparent from analysis of the amount of serum given to the various groups of children. This was brought out clearly in the cases in which blood titration was done. For instance, there was no greater increase in the serum titer of 2 children who received 30 cc., the maximum amount, of serum than in that of the 9 children who received the

minimum amount given in this series, 10 to 15 cc. The children of the older group, from 3 to 6 years of age, who received larger amounts of serum, did not fare any better than the younger children. Moreover, in another group of children it was possible to bring about a reversal of the Schick reaction by means of small amounts of serum of high titer.

As mentioned, central pallor in the area of the Schick reaction that occurred in some of the cases was of no value in the prediction of the subsequent reversal of the Schick reaction. It is of interest to point out that the phenomenon occurred only in 12 per cent of the repeated positive reactions and in 21 per cent of the original reactions.

Nine of the donors in this group whose serum failed to bring about a reversal of the cutaneous reaction had a positive Schick reaction. Unfortunately the other donors could not be given the Schick test. Apparently it can be assumed that the possibility of producing a reversal of the reaction by means of serum from a donor with a positive reaction to the Schick test or by that of a low titer from a donor with a negative Schick reaction is remote.

Cases in Which the Positive Schick Reaction Became Negative after Injection of Serum.—The data for analysis of the group whose Schick reactions became negative subsequent to injection of serum comprise 364 observations of Schick tests on 98 children ranging in age from 6 months to 12 years. In addition, blood titrations were done on 33 of this group. The data on 5 additional children who received one or more transfusions were discarded. The children in this series were also divided into 3 age groups: from 6 months to 3 years; from 3 years to 6 years, and from 6 to 12 years. The subjects for whom titrations were not done were about equally divided among the 3 age groups. Of the patients for whom titrations were done, two thirds, or 22 children, were under 3 years of age, in a period in which, owing to lack of experience with diphtheria toxin, there is usually slower development and a shorter duration of immunity. Such children, indeed, offer themselves as material for a rigid test of the efficacy of human serum to bring about a modification of the antitoxin level of the patients' serum and Schick reaction (tables 3 and 4). It is of interest to note that in the entire group of 98 children, 18 who received prophylactic injections of toxoid had positive Schick reactions before injection of human serum, and the duration of immunity after injection of serum was an average of four and six-tenths weeks, a period shorter than the average duration of the entire group.

As is shown in table 3, the children for whom titrations were done received on the average from 16 to 21 cc. of serum, individual children of this group receiving an amount as low as 10 to 15 cc., a smaller amount than that given the children for whom no titrations were made, who received 28 to 34 cc. of serum. As it happened, the latter group

TABLE 3.—*Summary of Observations on Patients Whose Positive Schick Reaction Became Negative After Injection of Serum (Patients on Whom Titrations Were Made)*

Age Group	Number of Children	Children Immunized Before Admission*	Serum Average (Cc.)	Schick Test Before Serum: Intensity: Degree	Schick Test Before Serum: Intensity: Number of Cases	Schick Test Before Serum: Central Pallor: Presence	Schick Test Before Serum: Central Pallor: Number of Cases	Schick Test After Serum: Number of Negative Schick Reactions, (Range)	Schick Test After Serum: Duration of Immunity, (Average Number of Weeks)	Subsequent Schick Reactions from Negative to Positive†: Intensity: Degree	Subsequent Schick Reactions from Negative to Positive†: Intensity: Number of Cases	Subsequent Schick Reactions from Negative to Positive†: Central Pallor: Presence	Subsequent Schick Reactions from Negative to Positive†: Central Pallor: Number of Cases	Titration of Serum (Average Units per Cc.): Donor	Titration of Serum (Average Units per Cc.): Patient Before Serum	Titration of Serum (Average Units per Cc.): Patient After Serum	Serum Injection to Second Titration, (Average Number of Days)	Second Schick Test to Second Titration, (Average Number of Days)
6 mo. to 3 yr.	22	3	21.7	+	12	No	13	1-3	9.6	+	9	No	9	0.0234	0.0036	0.0096	6.1	1.6
				++	9	....	..	...	....	++	0	....	..					
				+++	1	Yes	9	...	....	+++	0	Yes	0					
3 to 6 yr.	8	3	24.0	+	3	No	6	1-3	10.6	+	3	No	2	0.0250	0.0035	0.0116	5.2	1.1
				++	4	....	..	...	....	++	0	....	..					
				+++	1	Yes	2	...	....	+++	0	Yes	1					
6 to 12 yr.	3	0	16.6	+	1	No	3	1-3	10.0	+	1	No	1	0.0233	0.0036	0.0166	3.3	0.3
				++	2	....	..	...	....	++	0	....	..					
				+++	0	Yes	0	...	....	+++	0	Yes	0					

* By 2 or more previous injections of alum or toxoid.

† Nine children in the first age group, 3 in the second and 1 in the third were observed for intensity and central pallor.

TABLE 4.—*Summary of Observations on Patients Whose Positive Schick Reaction Became Negative After Injection of Serum (Patients on Whom Titrations Were Not Made)*

Age Group	Number of Children	Children Immunized Before Admission*	Serum Average, (Cc.)	Schick Test Before Serum				Schick Test After Serum		Subsequent Schick Test† from Negative to Positive			
				Intensity		Central Pallor		Number of Negative Schick Reactions, (Range)	Duration of Immunity, (Average Number of Weeks)	Intensity		Central Pallor	
				Degree	Number of Cases	Presence	Number of Cases			Degree	Number of Cases	Presence	Number of Cases
6 mo. to 3 yr.	25	2	34.6	+	16	No	20	1-3	8.7	+	11	No	15
				++	6	....	..			++	4	....	..
				+++	3	Yes	5			+++	0	Yes	0
3 to 6 yr.	21	1	29.9	+	12	No	7	1-5	16.2	+	7	No	8
				++	8	....	..			++	3	....	..
				+++	1	Yes	14			+++	0	Yes	2
6 to 12 yr.	19	9	28.8	+	12	No	10	1-3	15.3	+	10	No	9
				++	6	....	..			++	0	....	..
				+++	0	....	..			+++	0	Yes	1
				++++	1	Yes	9						

* By 2 or more previous injections of alum or toxoid.

† Fifteen patients in the first age group, 10 in the second and 10 in the third were observed for intensity and central pallor.

was studied during the fall and winter seasons and therefore additional amounts of serum were given in cases of pneumonia. Besides, in studying the cases in which titrations were done, an attempt was made to find the minimum amount of serum necessary to raise the antitoxic level of the blood and to modify the Schick reaction. Mention was previously made that small amounts of serum of high titer are just as effective in producing a reversal and a rise in titer as larger amounts of serum of low titer. This was brought out in the study of this group of cases, in which the results in 8 children who received between 10 and 15 cc. of serum of an average titer of 0.03 units per cubic centimeter were similar to those in 24 children who received 20 to 45 cc. of serum of an average titer of 0.0225.

In keeping with our experience in studying the previous group, the number of children in the present series who had central pallor in the original positive Schick reaction was 39, or 40 per cent, as compared with 8 per cent of the children with central pallor among those whose Schick reactions became positive after being negative for various intervals following serum injection.

That the Schick test itself, frequently repeated, may be a means of producing an antigenic reaction should be taken into consideration. Goldbloom,[5] for instance, found that when he repeated at intervals of a few days the Schick test of a child with a Schick-positive reaction, the fourth reaction became negative and the blood showed a titer above the immunity level. In 1922 Glenny[6] and in 1926 O'Brien[7] stated that the small amount of antigen present in the Schick test could be sufficient to stimulate formation of antibodies and that consequently a subsequent Schick reaction would be negative. We should like to emphasize at this point that in this series a reversal of the reaction took place in all cases on the first retest following the injection of serum and almost the entire group of children whose retests at various intervals gave a negative reaction had a positive reaction subsequently. Of the children with persistently positive reactions on whom repeated Schick tests were carried out in the same manner, 6 had more than one repeat test during the period of observation and no modification of the reaction was noted. Before leaving this phase of the subject we should like to mention the following facts: In the group of 33 cases in which titrations were done and in which a reversal took place, the interval between the second Schick test and the subsequent titration ranged from seven

5. Goldbloom, A., and Klein, L. D.: Diphtheria Immunization with Concentrated Toxoid Intradermally, J. Pediat. **3**:112 (July) 1933.

6. Glenny, A. T., and Allen, K.: The Schick Dose of Diphtheria Toxin as a Secondary Stimulus, J. Hyg. **21**:104, 1922.

7. O'Brien, R. A.: Immunity Produced by the Schick Test, J. Path. & Bact. **29**:320, 1926.

to thirty-eight hours, a period in which the toxin in the Schick material could not have caused a rise in the serum titer. In contrast, in 20 cases in which the serum did not produce a reversal of the reaction, the interval between the retest and the second titration was from fifty-three to sixty-two hours, without causing an appreciable rise in titer, a long enough period for the toxin in the Schick material to cause a modification of the Schick reaction as well as a rise in the serum titer. In view of those facts, the results obtained in both groups are undoubtedly due to the injection of serum.

A factor which serves to confuse the question of immunity to diphtheria, as indicated by the Schick test, is the fact that patients in a ward may come in contact with diphtheria carriers from time to time and thus build up an immunity to diphtheria. It may be well to point out here that persons without artificial immunity who gave positive Schick reactions may in the course of time have negative reactions. This is particularly true among children and adults in a thickly populated urban area. Cultures of material from the nose and throat were made routinely for every patient admitted to the ward, and in no instance was a diphtheria carrier discovered. During the entire period of this study only 1 patient with diphtheria happened to be inadvertently admitted to the ward. We can safely state, therefore, that no factor but injection of human serum was responsible for the reversal of the Schick reaction in this series of cases.

Von Behring,[8] Zingher[9] and Kojis and Craig[10] have suggested that there is a temporary loss of natural immunity to diphtheria during the acute febrile stage of a disease. This explains the greater prevalence of clinical diphtheria among patients with scarlet fever. The high incidence of positive Schick reaction in our series was mainly among patients of the younger age group, who had not yet acquired an active immunity either by means of contact or by toxoid immunization. Moreover, we were able to bring about a negative Schick reaction by means of injection of serum even during the febrile stage of the disease, and in those in whom serum failed to produce a reversal the Schick reaction remained persistently positive long after the patient recovered.

Blood Titration.—Recently the question has been raised as to whether the Schick reaction is merely an accompanying phenomenon or an absolute and essential condition of the changed state of suscepti-

8. von Behring, E.: Ueber ein neues Diphtherieschutzmittel, Deutsche med. Wchnschr. **39**:873, 1913.

9. Zingher, A.: The Schick Test in Poliomyelitis, Scarlet Fever, Malaria and in Normal Children, Am. J. Dis. Child. **13**:247 (March) 1917.

10. Kojis, T. G., and Craig, J. D.: Effect of Scarlet Fever on Immunity to Diphtheria as Determined by Schick Test, Am. J. Dis. Child. **49**:383 (Feb.) 1935.

bility. In fact, the test has not been recognized by some as a valid procedure in the evaluation of immunization; they feel that blood titration gives more information concerning the immunization response than does the Schick test. Jensen [11] showed that healthy young children may give a negative reaction and yet may have little antitoxin in the blood. Flood [12] expressed the opinion that the Schick test is misleading. On the other hand, Schick [13] has often been quoted from his original work as saying that a person requires one thirtieth of a unit of antitoxin per cubic centimeter of serum in order to give a negative reaction. Messeloff and Karsh [14] corroborated the value of the Schick test in blood titration studies. They found that of 57 children with negative reactions, 48 had at least one thirtieth of a unit of antitoxin in the blood. Schick, Van Gröer and Kassowitz [15] in a later study found negative Schick reactions to as low as 0.005 unit of antitoxin per cubic centimeter. Recent studies in this field by Brandon and Fraser,[16] Fraser and Halpern,[17] and Parish and Wright [18] have established a much lower figure. They expressed the belief that a negative Schick reaction may be produced by serum containing 0.002 to 0.004 unit per cubic centimeter. It has been shown that there is no definite level of serum antitoxin above which the reaction is negative and below which the test is positive. From the literature just referred to it is evident that a marked divergence of opinion exists regarding correlation of results of titration studies with those of the Schick test.

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11. Jensen, C.: Sur l'importance de la reaction de Schick négative chez les enfants non immunisés avec l'antitoxin diphthérique, Compt. rend. Soc. de biol. **108**:555, 1931.

12. Flood, R. A.: Blood Diphtheria Antitoxin Studies, Am. J. Dis. Child. **39**:107 (Jan.) 1930.

13. Schick, B.: Determining Immunity Against Diphtheria, Weekly Bull. New York Dept. Health (Jan. 5) 1929. Park, W. H., and Dickerson, A. J., in Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1925, vol. 6, p. 96.

14. Messeloff, C. R., and Karsh, M. J.: Antitoxin Content of the Blood Serum of Children with Negative Reaction to the Schick Test, Am. J. Dis. Child. **44**:999 (Nov.) 1932.

15. Schick, B.; Van Gröer, F., and Kassowitz, K.: Methodik und Technik des Erforschung der normalen antitoxischen Diphtherieinmmunität des Menschen, in Abderhalden, E.: Handbuch der biologischen Arbeitsmethoden, Berlin, Urban & Schwarzenberg, 1924, vol. 1, sect. 13, pt. 2, p. 531.

16. Brandon, K. F., and Fraser, D. T.: Observations on the Interpretation of Schick Tests, J. Immunol. **31**:387 (Nov.) 1936.

17. Fraser, D. T., and Halpern, K. C.: Diphtheria Toxoid, Canad. Pub. Health J. **26**:469 (Oct.) 1935.

18. Parish, H. J., and Wright, J.: The Schick Test and Active Immunization in Relation to Epidemic Diphtheria. Lancet **1**:600 (March 16) 1935.

Our experience in this connection can be summarized by the findings in table 5; namely, there was a high correlation between the rise in the serum titer and the reversal of the positive Schick reaction. We found the Schick test a practical method for the determination of susceptibility to diphtheria. A negative Schick reaction may certainly be taken at least as presumptive evidence of immunity to diphtheria.

Titration studies were done on 55 children. Of 33 in whom the serum brought about a reversal of the Schick reaction, there was a significant rise in titer in 91 per cent. Of 22 children in whom the serum failed to produce a negative Schick reaction, there was only a slight rise in titer in 40 per cent. Since definite conclusions could not be drawn from the small number of cases in the older age groups, table 5 represents the analysis of results of titration studies of 39 children ranging in age from 6 months to 3 years. The average original titer of the blood of the patients whose Schick reaction became negative was 0.0036 unit per cubic centimeter and 0.0096 unit per cubic centimeter after injection of serum, a rise of 0.006 unit, or of 166.6 per cent. In contrast, 17 children whose Schick reaction remained positive after injection of serum and whose original titer was exactly the same as that of the former group of children, 0.0036 unit per cubic centimeter, the rise following injection of serum was only 0.0016 unit, or 44.4 per cent. Attention should be called to the fact that the titer of the donors' serum given to the first group was 0.0047 unit per cubic centimeter higher than that given to the second group. These observations would indicate that the higher potency of the serum brought about a reversal of the reaction to the Schick test as well as a rise in titer above that associated with the negative Schick reaction. In the group with persistently positive Schick reactions, though there was a slight rise in titer it was not enough to cause a reversal, but it was enough to reduce the intensity of the reaction to the Schick retest.

TABLE 5.—*Comparison Between the Titer of Patients Whose Schick Reaction Became Negative and Those Whose Schick Reaction Was Persistently Positive After Injection of Serum*

Group	Number of Children	Average Age (Mo.)	Titration of Serum—Units per Cc. (Average)			
			Before Serum	After Serum	Percentage of Increase	Difference
Whose Schick reaction became negative	22	15.3	.0036	.0096	166.6	.006
Whose Schick reaction remained persistently positive	17	21.8	.0036	.0052	44.4	.0016

As has already been pointed out in connection with the effect of the Schick reaction or its subsequent reversal, the importance of the Schick test in influencing the titer has also been considered. Parish

and Wright [19] expressed the belief that the performance of the test followed by titration was responsible for the many abnormally high levels for normal limits of a negative Schick reaction. To obviate such a possibility, they performed the titration first and then they did the Schick test. Despite the fact that in our study the test was done first, we did not find abnormally high levels in the blood titer. In 24 of 33 children the titer was 0.003 unit per cubic centimeter. Sixteen of this group were less than 3 years of age. The children's lack of experience with diphtheria antitoxin during this period is undoubtedly responsible for the lack of rise in titer which a small amount of antigen present in the Schick test will produce. Moreover, Fraser and Halpern [20] have pointed out that the response of the humoral mechanism to the Schick test is rather slow in raising the titer, the maximum response in certain cases being reached only after several weeks. Consequently, the interval of from three to five days that elapsed between the Schick test and the administration of the serum was not long enough to stimulate the formation of enough antitoxin to raise the titer and produce a reversal of the test.

COMMENT

Aside from the theoretic aspects of immunity, the form of the immunologic agent employed is of considerable importance from the practical point of view. In certain municipal hospitals the patients newly admitted to the ward are inoculated with from 1,000 to 2,000 units of diphtheria antitoxin as a prophylactic measure. This renders the patient passively immune against diphtheria only for ten to twenty-one days. It must be borne in mind that such a procedure sensitizes the patient to foreign proteins and that there is a possibility of an occurrence of an aphylactic reaction caused by subsequent injections of animal serum.

As pointed out elsewhere, the average stay of the children in the hospital is about three weeks, ranging from a few days to three months. It was important, therefore, to take into consideration the rate of development of immunity; the prophylactic agent employed must be capable of producing immunity in the shortest period of time and the development of immunity should at least approximate that of the incubation period of the disease. In addition, the agent employed must be free from the objectionable features associated with the use of animal serums and should be capable at the same time of producing protection not only against diphtheria but against other infectious diseases as well. All these objectives were attained by means of human serum.

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19. Parish, H. J., and Wright, J.: Schick Reaction and Circulating Diphtheria Antitoxin in Man, Lancet **1**:882 (April 16) 1938.

20. Fraser, D. T., and Halpern, K. C.: Serial Titrations of Diphtheria Antitoxin Following Toxoid, Canad. Pub. Health J. **26**:476 (Oct.) 1935.

The interval between the administration of the serum and the second titration in 33 cases varied from three to eighteen days. There was no appreciable difference in the titer between those cases in which the titration was made after eighteen days and the 18 cases in which the determination was done three to four days after the injection of serum. It is quite possible that the same result would have been obtained had the determination been made sooner. On the basis of such observations, we believe that the immunity conferred by human serum develops rapidly enough to insure protection.

That human serum may possess some special quality was indicated by Thelander's [21] experience. She stated that during an epidemic of poliomyelitis, children who received human serum gave a negative Schick reaction later; those who received animal serum did not. She obtained a reversal of the Schick reaction with as low as 6 cc. of blood or 2.5 cc. of serum without a rise in titer above the Kellogg level.[22] However, her studies do not indicate whether there was any rise at all in the titer. It can be easily seen that under such circumstances, even though the blood must have had some potency to produce a negative reaction, a correlation between the Schick reaction and the titer could hardly be expected. The fact that a reversal of the reaction was obtained by means of such a small amount of serum is extremely interesting. None in our series received such small amounts of serum; the minimum given to some children was 10 cc. It is of interest to point out that even in the group of patients in whom the Schick reaction remained positive, some had a small but definite rise in titer, which may have accounted for the lesser intensity in the Schick reaction subsequent to the injection of serum.

It is important to bear in mind that there is a wide variation in the antitoxin content of the blood in different persons who react negatively to the test. Just what constitutes an adequate, or minimal, prophylactic dose in a given case or whether smaller amounts of serum will produce the same results, we are unable to say.

The problem that interested us particularly was that of the duration of the immunity and the mechanism by which human serum raises the titer of the blood which lasts for variable periods. Does the serum act by virtue of its antibody content only, or does it also exert its activity as a humoral stimulant, activating the tissues to produce antibodies which in some cases render the person immune for a long time? This

21. Thelander, H. E.: Individual Variations in Immunity, Am. J. Pub. Health **25**:737 (June) 1935.

22. Kellogg, W. H., and Stevens, I. M.: Some Observations Regarding Diphtheria Immunity, J. A. M. A. **89**:273 (July 23) 1927.

TABLE 6.—*Comparison of Duration of Immunity Among the Patients With Negative Schick Reactions*

Age Group	Total Number of Children with Original Positive Schick Reaction	Number of Children Whose Schick Reaction Became Negative	Percentage of Children Whose Schick Reaction Became Negative	Duration of Immunity						
				Average (Weeks)	Six Weeks or Less			Longer than Six Weeks		
					Number of Children	Percentage of Children	Average Duration (Weeks)	Number of Children	Percentage of Children	Average Duration (Weeks)
6 mo. to 3 yr.	72	47	65.2	9	21	44.6	3	26	55.4	13.9
3 to 6 yr.	40	29	72.5	14.7	11	37.9	3.3	18	62.1	22.3
6 to 12 yr.	29	22	75.8	14.6	11	50.0	3.3	11	50.0	26.
Total.....	141	98	69.6	12.2	43	43.9	3.2	53	56.1	20.5

point is raised with regard to those persons in whom the reversal of a positive Schick reaction produced by human serum persists for eight months or longer.

It was essential for us to determine the duration of immunity conferred by human serum, for if the duration is shorter than the average stay of the patient in the hospital it would entail the necessity of administering serum at frequent intervals, a serious objection to its routine use. Analysis of 98 cases in which the Schick reaction was negative (table 6) reveals that in 55 cases, or 56.1 per cent, the duration of immunity ranged between eight and fifty-six weeks, an average duration of twenty and five-tenths weeks. In 43 cases, or 43.9 per cent, the duration was from two to six weeks, an average of three and two-tenths weeks. From these observations it is evident that more than half of the patients were protected by means of serum during their maximum stay in the hospital. The remaining number were protected at least for the average stay in the institution.

It is to be noted from table 6 that injection of serum brought about a reversal of the reaction in 65 per cent of a total of 72 children in the lowest age group, as compared with the two older age groups, in whom a reversal of the reaction was obtained in 72.5 per cent and 75.8 per cent of the children respectively. The average duration of immunity, as determined from the period of our observation, was longer in the two older age groups than in the children of 6 months to 3 years of age. When we considered the persons whose immunity lasted more than six weeks, we found that the protection conferred by the serum lasted only thirteen weeks in the youngest age group, as compared with twenty-two and twenty-six weeks in the two older groups. These observations would tend to indicate that the youngest age group, in which the smallest percentage of children were protected, lost its immunity sooner.

The immunity produced by means of human serum persisted in some cases for as long as eight months, as compared with that obtained by diphtheria antitoxin, which lasts about three weeks. Apparently in homologous serum, as pointed out by Baar,[23] the antibodies are retained in appreciable amounts for a considerable time, while in diphtheria antitoxin, heterologous serum, the antibodies are rapidly eliminated.

SUMMARY

Because of the fact that susceptibility of a person to diphtheria can be determined within twenty-four hours by means of the Schick test and blood titration, diphtheria was singled out from other con-

23. Baar, H.: Vergleichende Untersuchungen über die Wirkung homologer und heterologer Sera bei der Diphtherie, Klin. Wchnschr. **11**:1545 (Sept. 10) 1932.

tagious diseases for special study to determine the mechanism by which the routine injection of human serum prevents the development of secondary contagious diseases in a hospital ward.

This investigation is based on observations of the effect of human serum on the cutaneous reaction in 141 children with positive reaction to the Schick test and on the blood titer of 55 of this group.[1] The children ranged in age from 6 months to 12 years. The Schick test was performed on every patient admitted to the hospital and a retest was given within several days after the serum injection. Subsequent retests, at monthly intervals, were carried out on patients in whom a reversal of the reaction followed serum injection. Intramuscular injection of from 10 to 30 cubic centimeters of human serum was given to every patient within twenty-four hours after admission. Within twenty-four hours after the serum injection a central pallor developed in the area of the Schick reaction and within forty-eight hours there was a clear demarcation between the central pallor and the peripheral inflammatory zone. In patients to whom serum was not given this phenomenon did not occur. This anomaly did not indicate that a subsequent reversal of the Schick reaction would take place.

Injection of human serum brought about a reversal of the Schick reaction in 98 children, or 69.6 per cent. In 43 children, or 29.4 per cent, the Schick reaction remained persistently positive despite the serum injection. The intensity of the Schick reaction, however, apparently was reduced by means of the human serum. The modification of the reaction of 8 children who received from 10 to 15 cc. was similar to that of 24 children who received from 20 to 45 cc. of serum.

Titration studies were done on 55 children. Of 33 children in whose Schick reaction the serum brought about a reversal there was a significant rise in titer in 91 per cent, while of 22 whose Schick reaction was persistently positive there was only a slight rise in titer in 40 per cent. There was a close correlation between the rise in serum titer and the reversal of the positive Schick reaction. Analysis is presented of the observations on 39 children of the youngest age group, in whom 22 whose Schick reaction became negative after injection of serum had a rise in titer of 166.6 per cent, as compared with a rise of 44.4 per cent in 17 children whose Schick reaction was persistently positive. The average titer of the donors' serum in the former group was 0.0047 unit per cubic centimeter higher than the amount of the serum given to the latter group. These observations would indicate that the higher potency of the serum was responsible for the reversal of the Schick reaction as well as for the rise in titer of the patients' blood. In this study the repetition of the Schick test was not responsible for the rise in the blood

titer or for the reversal of the reaction, as the interval between the second test and the subsequent titration ranged between seven and thirty-three hours, a period in which the Schick material could not be a factor.

Human serum protected more than half of the children for twenty and five-tenths weeks and the remainder for three and two-tenths weeks. The average period of protection was thirteen weeks in the cases of the youngest group of children, as compared with twenty-two and twenty-six weeks in those of the two older groups. It was found that the youngest age group, in which the smallest percentage was protected, lost its immunity sooner.

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PARANASAL SINUSES FROM BIRTH TO LATE ADOLESCENCE

I. SIZE OF THE PARANASAL SINUSES AS OBSERVED IN ROUTINE POSTEROANTERIOR ROENTGENOGRAMS

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DENVER

The paranasal sinuses in infancy and childhood have been of interest to the medical profession for many years. The embryology and development of the sinuses have been investigated and reported completely. Sinus infection in children and its relationship to general health, pulmonary disease and growth of the sinuses have been the subject of numerous reports. Most of the literature has dealt with anatomic material and with patients seen in clinics and in practice. There have been few reports on the sinuses of normal children.

For many years the Child Research Council has been collecting data on a group of healthy children. As part of that program, routine roentgenograms of the sinuses and of the chest have been taken, physical examinations recorded and the interval history noted periodically from the time the child is born. Since each child is examined at approximately three month intervals, a large amount of material is now available for analysis.

The present report will deal, first, with the increase in size of the sinuses as evidenced in the routine posteroanterior roentgenograms and, second, with the variations in size of sinuses at different age levels. Although many of the variations are of little significance to the clinician, there is a great deal of interesting information brought forth by such continual observations of individual children.

The second part of this study will appear at a later date. In it the appearance of the sinuses in the roentgenograms, the clinical findings in the nose, throat, and chest, the interval history and the appearance of the pulmonary fields in the roentgenograms of the chest from the child's birth to his present age will be discussed and possible correlations made. Since the records on these children cover many years and have been continuous, we hope to present much of interest to the pediatrician, the otolaryngologist and the roentgenologist.

From the Child Research Council and the University of Colorado School of Medicine.

REVIEW OF THE LITERATURE

Many papers on the paranasal sinuses are published yearly. Of these only a few are significant. After reviewing some of the literature that has been presented during the last decade, one feels that one can agree wholeheartedly with Smyth's [1] statement: "The volume of literature on the sinuses during the past year is as usual abundant and also as usual

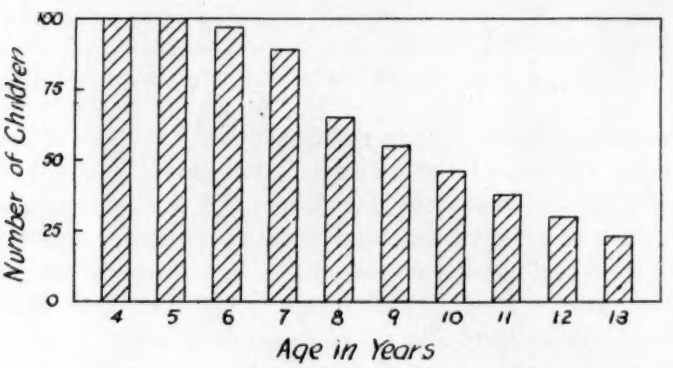

Fig. 1.—Numbers of children followed and ages covered by the observations in the study of the time of appearance of frontal sinuses above orbital roofs as seen in roentgenograms.

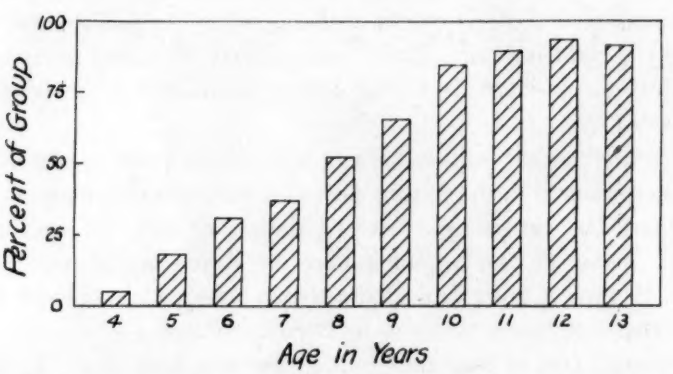

Fig. 2.—Percentage of children in each age group shown in figure 1 who had one or both frontal sinuses at the level of or above the orbital roof in the roentgenograms at the indicated ages.

contains little that is new." I shall not attempt to summarize or discuss the literature at any great length but shall simply mention some of the articles that concern the development of the sinuses.

1. Smyth, D. C.: Paranasal Cavities: Review of the Literature from October 1, 1928, to October 1, 1929, Arch. Otolaryng. **12**:89 (July) 1930.

The earliest report of the use of the roentgenogram in determining the presence or size of the paranasal sinuses and in diagnosing antral sinusitis was by Scheier [2] in 1896. Philip,[2] of San Francisco, was the first American to report on roentgenography of a sinus. Since the time of that report (1902) the roentgenogram has become a valuable adjunct in the diagnosis of sinus disease. It has also been of great importance to the physician and to the surgeon in determination and delineation of anatomic conformations. All writers agree that there is no constant, or so-called "normal," type in the anatomy of the paranasal sinuses. J. Parsons Schaeffer [3] in 1920 said, "It is therefore clearly obvious that the adherence to a single fixed and arbitrary normal is fraught with danger since with variations come altered size, altered shape, altered anatomic relations."

There have been many conflicting reports regarding the factors which bring about the pneumatization of the paranasal sinuses. Killian [4] is one

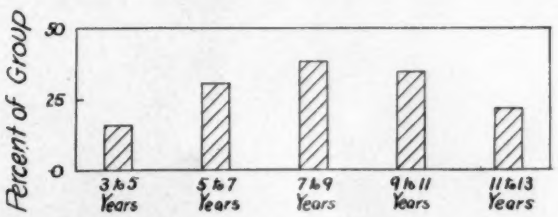

Fig. 3.—Time of appearance of frontal sinuses above orbital roofs in roentgenograms of the children represented in figures 1 and 2. The chart indicates the percentage distribution of the children according to the age intervals during which one or both frontal sinuses first reached the level of the orbital roofs. The number of cases in each age group corresponds to ages 5, 7, 9, 11 and 13 in figure 1.

of those who have expressed the belief that the development of sinuses depends on inherent biologic characteristics of cells which make up this area. Coffin and Freres [4] and others have explained the pneumatization of sinuses on a physical basis—the bone resorption being due to variations in air pressure, particularly that of expiration, since the principal growth of the sinuses occurs after breathing begins.

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2. Cited by Gafafer, W. M.: Transillumination and Roentgenography of Maxillary Sinuses, Arch. Otolaryng. **14**:737 (Dec.) 1931.

3. Schaeffer, J. P.: The Nose, Paranasal Sinuses, Nasolacrimal Passageways and Olfactory Organ in Man, Philadelphia, P. Blakiston's Son & Co., 1920.

4. Cited by Oppenheimer, S.: Accessory Nasal Sinuses of Children, J.A.M.A. **73**:656 (Aug. 30) 1919.

Van Gilse [5] expressed the belief that the development of the neosinus from the paleosinus takes place through the pneumatizing drive of the mucous membrane into the bone. When this tendency is interfered with, he said, the bone in that vicinity may yield to the mucosa of a neighbor-

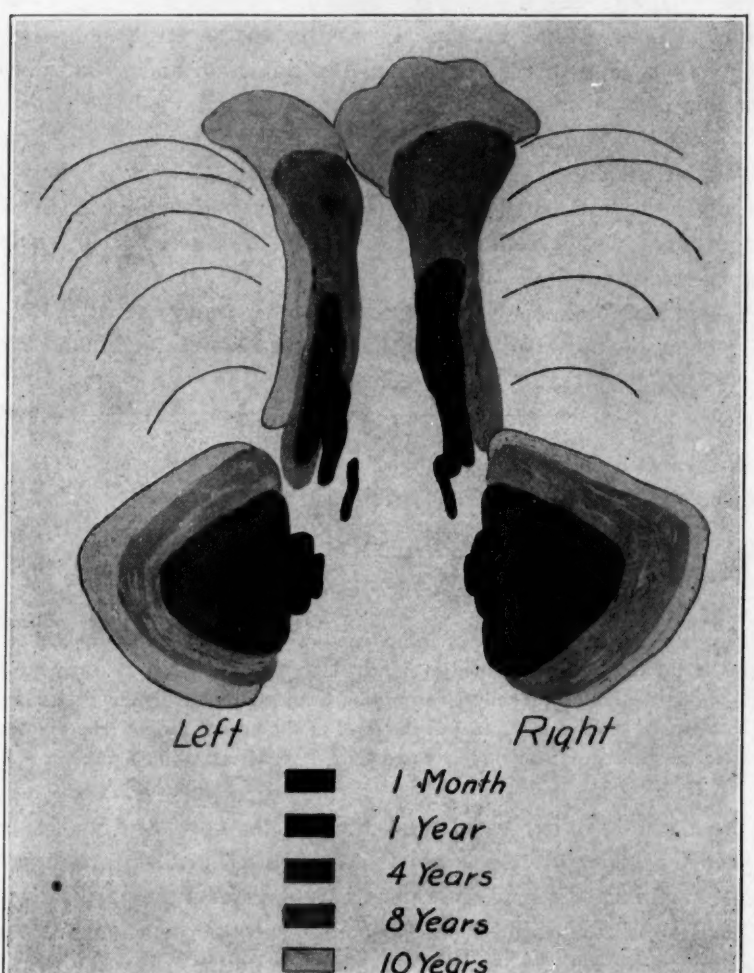

Fig. 4.—Composite drawing showing size and growth of the sinuses in D. I. (actual size of the tracings from the roentgenograms at each age represented).

ing sinus, thus resulting in a "battle for space." Sitsen [6] disagreed with this and said that there is no evidence of any pneumatizing influence in the mucosa itself. In his opinion the development of the frontal sinus in due to resorption of substantia spongiosa and the motive force comes

5. Van Gilse, P. H. G.: Acta oto-laryng. **22**:468, 1935.
6. Sitsen, A. E.: Arch. f. Ohren-, Nasen- u. Kehlkopfh. **140**:79, 1935.

from positive air pressure occurring during the respiratory cycle. He said that the great variability of frontal sinuses can be explained on the one hand by the action of the air pressure and on the other by differences in structure of the frontal bone. Richter [7] also stated that the stimulus

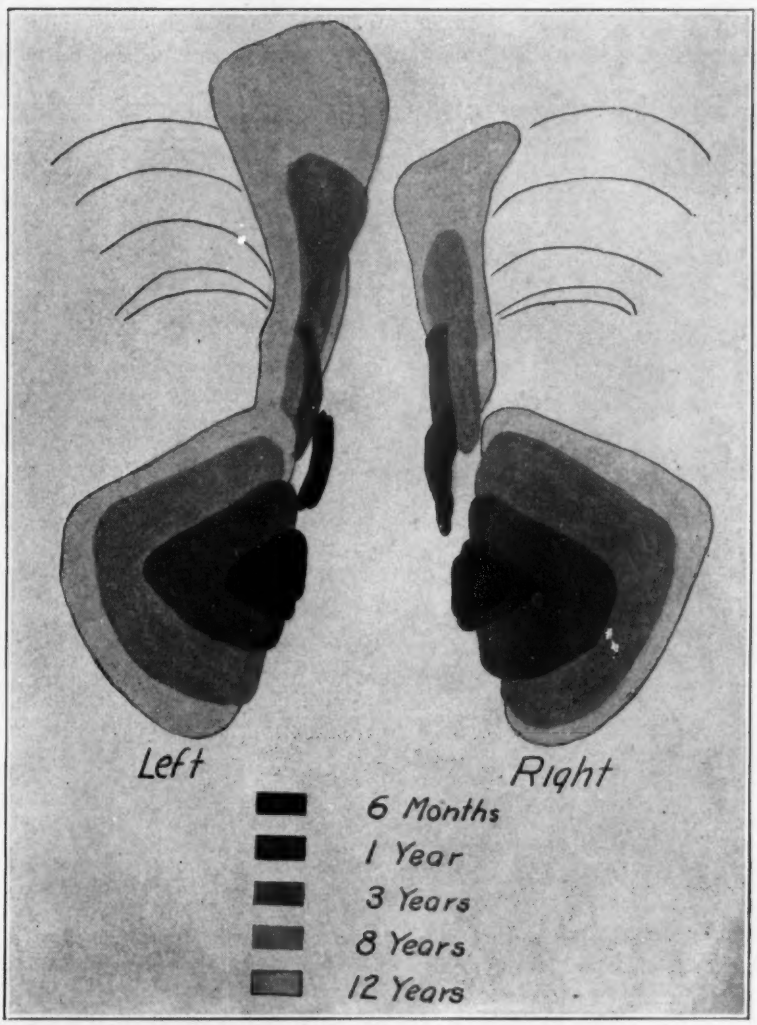

Fig. 5.—Composite drawing showing size and growth of the sinuses in M. S. (actual size of the tracings from the roentgenograms at each age represented).

for pneumatization goes out from the mucous membrane and that since some sinus development occurs in fetal life, air pressure as an influencing factor is out of the question. While, he said, the influence of external

7. Richter, H.: Arch. f. Ohren-, Nasen- u. Kehlkopfh. **141**:54, 1936.

air pressure on growth of the sinuses after birth cannot be definitely denied, neither can such an influence be definitely proved.

Grahe [8] in 1931 did experimental work with rabbits to find some factors influencing development of the nasal sinuses. He took out the molar teeth of 6 young rabbits and sewed up the external nares on one side in 6 more rabbits. Four months later the corresponding antrums were undeveloped in the 6 rabbits whose molar teeth had been extracted.

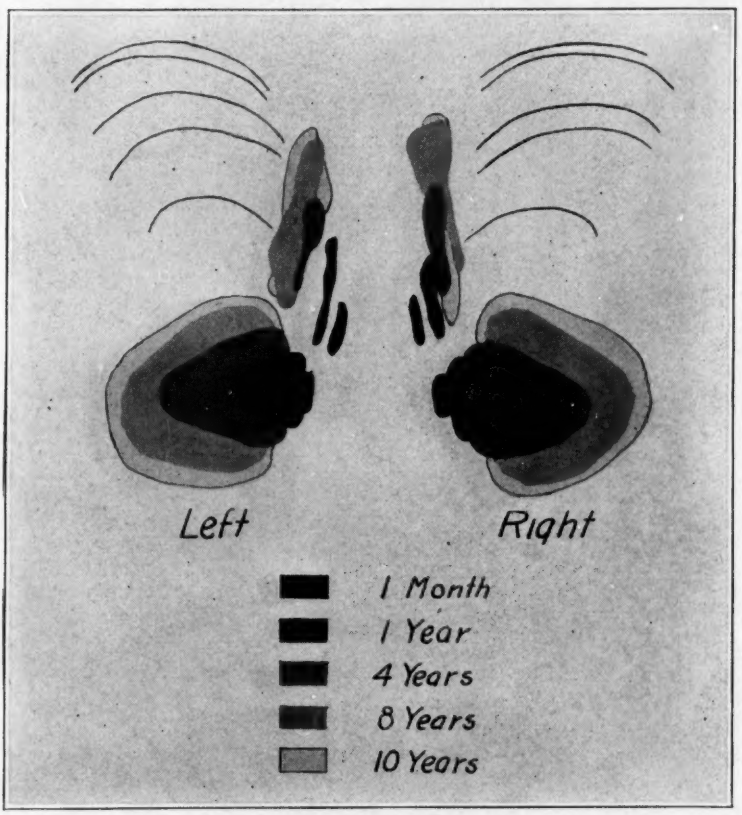

Fig. 6.—Composite drawing showing size and growth of the sinuses in R. Q. (actual size of the tracings from the roentgenograms at each age represented).

The rabbits whose external nares had been sewed up showed no abnormalities of antral development. In 1 rabbit in each series a severe unilateral suppurative sinusitis was found. In both animals the maxillary sinus was less developed on the infected side. Grahe inferred that growth of the alveolus is the principal influence on the development of the antrums.

8. Grahe, K.: Acta oto-laryng. **15**:141, 1931.

Carmody [9] expressed the opinion that infection of the maxillary and ethmoid sinuses early in life interferes with development of the frontal sinuses. From measurements of frontal sinuses of 262 normal persons, Palmer [10] found that the size of the sinus bears no relationship to the

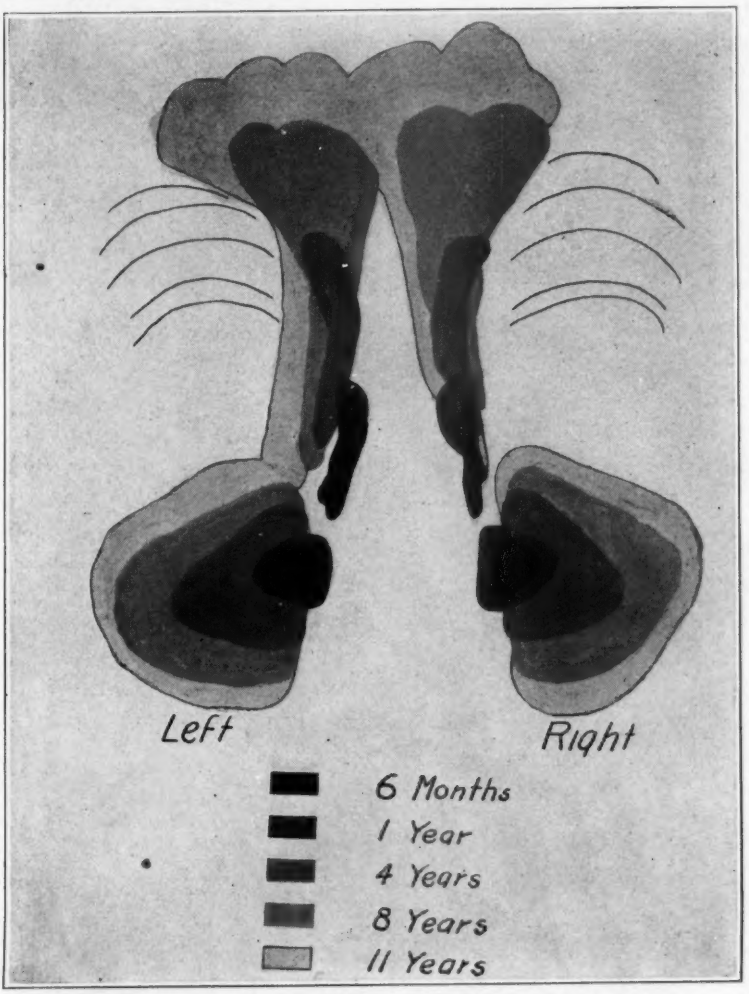

Fig. 7.—Composite drawing showing size and growth of the sinuses in W. S. (actual size of the tracings from the roentgenograms at each age represented).

number or duration of attacks of coryza. Shea [11] said that heredity is the greatest factor in determining the size and shape to which sinuses

9. Carmody, T. E.: Ann. Otol., Rhin. & Laryng. **38**:130, 1929.
10. Palmer, C. E.: Am. J. Hyg. **16**:224, 1932.
11. Shea, J. J.: Morphologic Characteristics of Sinuses, Arch. Otolaryng. **23**: 484 (April) 1936.

are destined to develop. He expressed the opinion, however, that a single severe infection or multiple mild infections may arrest the growth of the sinuses. Tanturri [12] said that he felt certain from his study of adults and of newborn infants with poorly developed sinuses and from his experimental work on animals that trauma at birth or in infancy

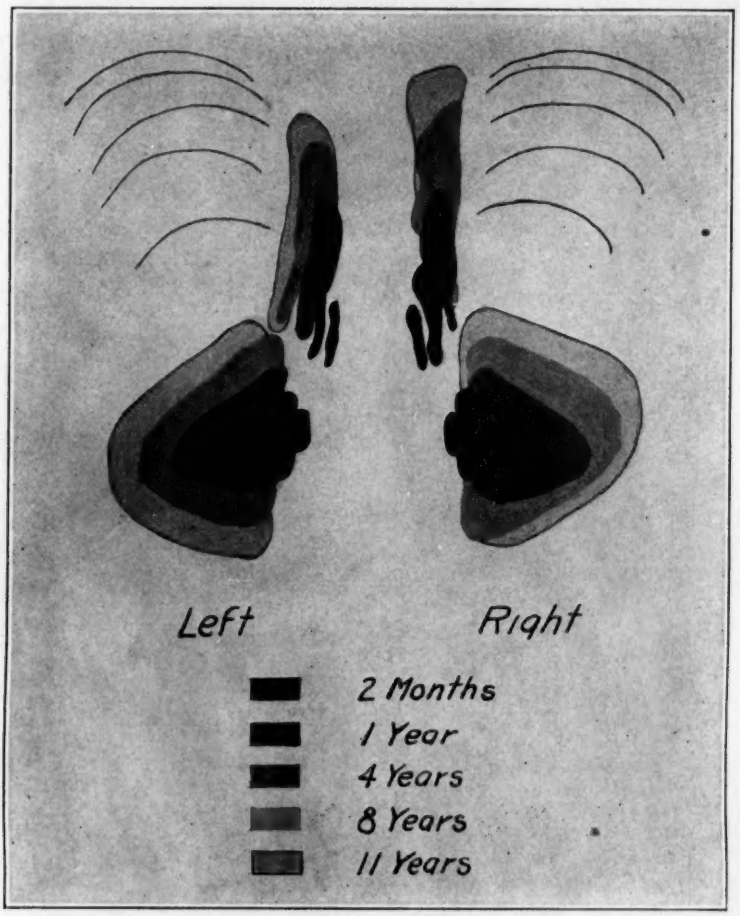

Fig. 8.—Composite drawing showing size and growth of the sinuses in C. S. (actual size of the tracings from the roentgenograms at each age represented).

causes a retardation in the development of the sinuses. After varying degrees of traumatization of experimental animals, he was able to demonstrate extravasations and inflammatory exudates extending into the

12. Tanturri, V.: Rassegna ital. d'ottal. **8**:193, 1935; abstracted, Zentralbl. f. Hals-, Nasen- u. Ohrenh. **25**:34, 1935; cited by Salinger, S.: Paranasal Sinuses, Arch. Otolaryng. **24**:204 (Aug.) 1936.

centers of ossification, although the mucosa showed a remarkable tendency to recover after severe trauma. After three or four months the affected sinus was definitely underdeveloped as compared with the opposite side. Schaeffer [3] found the growth of the antrums to be fairly

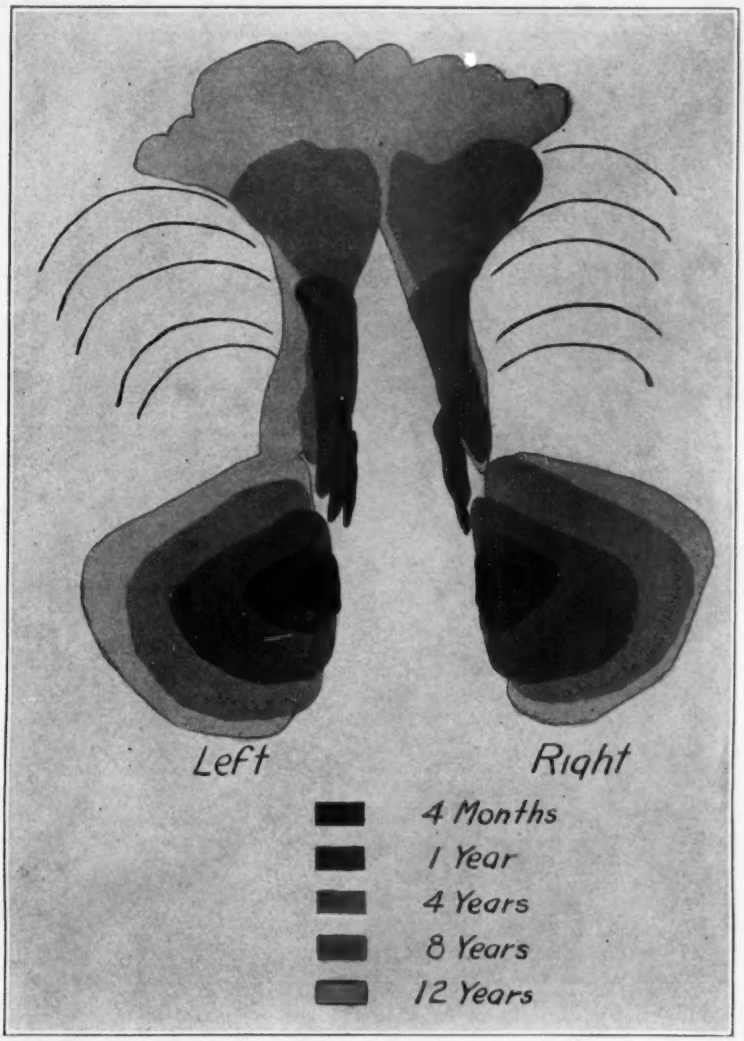

Fig. 9.—Composite drawing showing size and growth of the sinuses in A. H. (actual size of the tracings from the roentgenograms at each age represented).

uniform and little influenced by first dentition. He said that the age of the child, dentition and size of the sinus progress "pari passu."

Aplasia of the sinuses has been reported in varying percentages by different writers. The average is about 5 per cent of subjects with

aplasia of both frontal sinuses and 11.5 per cent with aplasia of one frontal sinus only, as reported by Haas.[13] Haas found underdeveloped frontal sinuses in 30.4 per cent and hypoplasia of the maxillary sinuses in 6.3 per cent of his patients. He expressed the opinion that one should

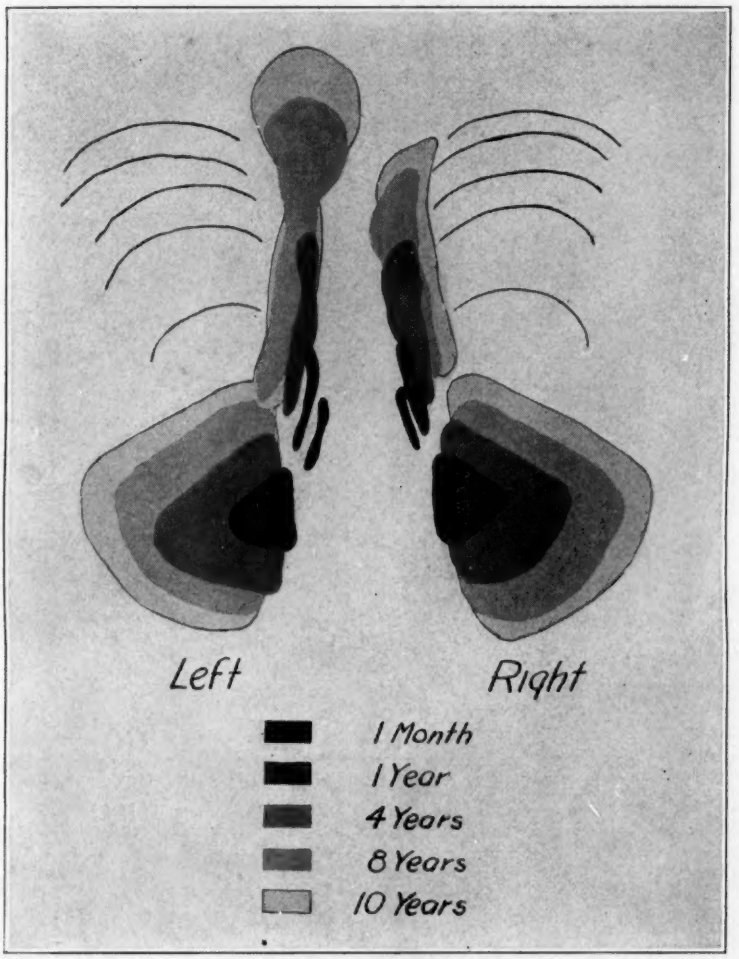

Fig. 10.—Composite drawing showing size and growth of the sinuses in R. S. (actual size of the tracings from the roentgenograms at each age represented).

stop considering aplasia and hypoplasia as congenital changes and rather consider them as secondary changes due to infection.

Warren Davis[14] in 1918 found on dissecting 160 specimens from subjects ranging in age from newborn infants to persons 16 years of age

13. Haas, L.: Monatschr. f. Ohrenh. **68**:1080, 1934.
14. Davis, W. B.: Ann. Otol., Rhin. & Laryng. **28**:940, 1918.

that in the average person the frontal sinus begins its ascent into the vertical portion of the frontal bone during the second year, is 3.8 mm. above the nasion at 3 years and continues its vertical advance at an average rate of 1.5 mm. per year till the fifteenth year. According to

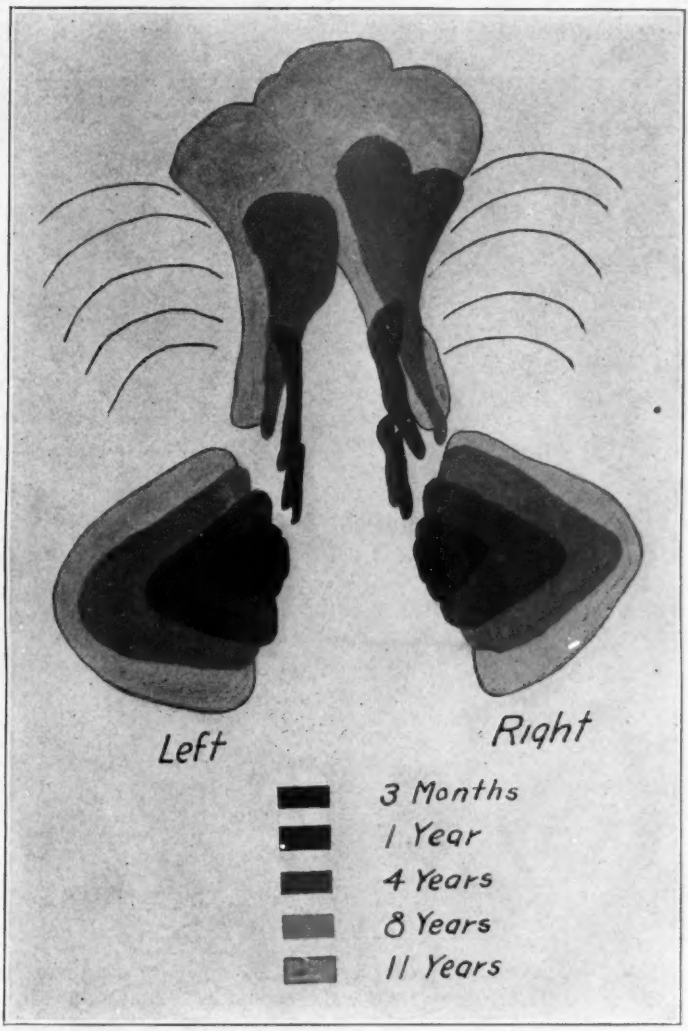

Fig. 11.—Composite drawing showing size and growth of the sinuses in M. W. (actual size of the tracings from the roentgenograms at each age represented).

Schaeffer,[3] the frontal sinus begins to develop in the region of the frontal recess of the middle nasal meatus during the fourth or fifth month of fetal life, but is not topographically frontal until some time after birth. It develops slowly till the seventh or eighth year and then more rapidly up to the twentieth year and increases somewhat in size up to old age.

Later in Jackson and Coates' book, Schaeffer [15] modified these statements by saying that by the end of the second year the frontal sinus has grown into the vertical portion of the frontal bone; that by the sixth year the cupola of the frontal sinus extends well above the nasion, and that at 8 years the normal variations being borne in mind, the frontal sinus may be considered of adult dimensions. According to Shea,[11] if

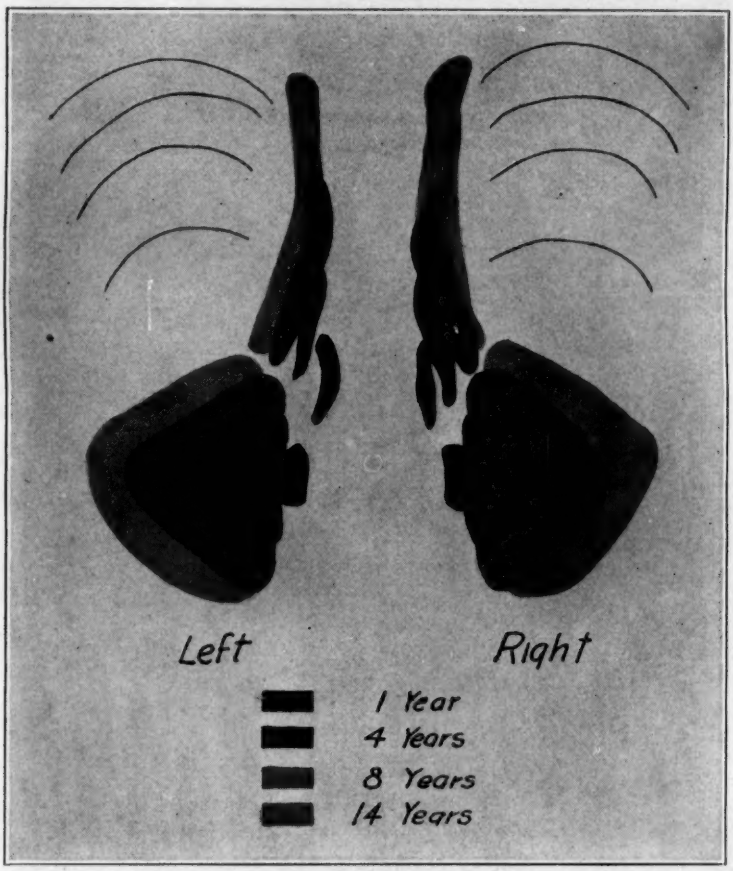

Fig. 12.—Composite drawing showing size and growth of the sinuses in B. S. (actual size of the tracings from the roentgenograms at each age represented).

the upward migration of the anterior ethmoid cell into the frontal bone is delayed beyond the fourth year, the sinus does not mature to natural size unless pneumatization is stimulated.

15. Schaeffer, J. P., in Jackson, C., and Coates, G. M.: The Nose, Throat and Ear and Their Diseases, Philadelphia, W. B. Saunders Company, 1929.

Anatomic investigators do not agree as to the time when the frontal sinus is mature. Hartmann and Milhalkovics [16] expressed the opinion that the frontal sinus does not cease expanding before puberty; Engel and Tillaux [16] placed the age at 12 years; Onodi and others [16] said they

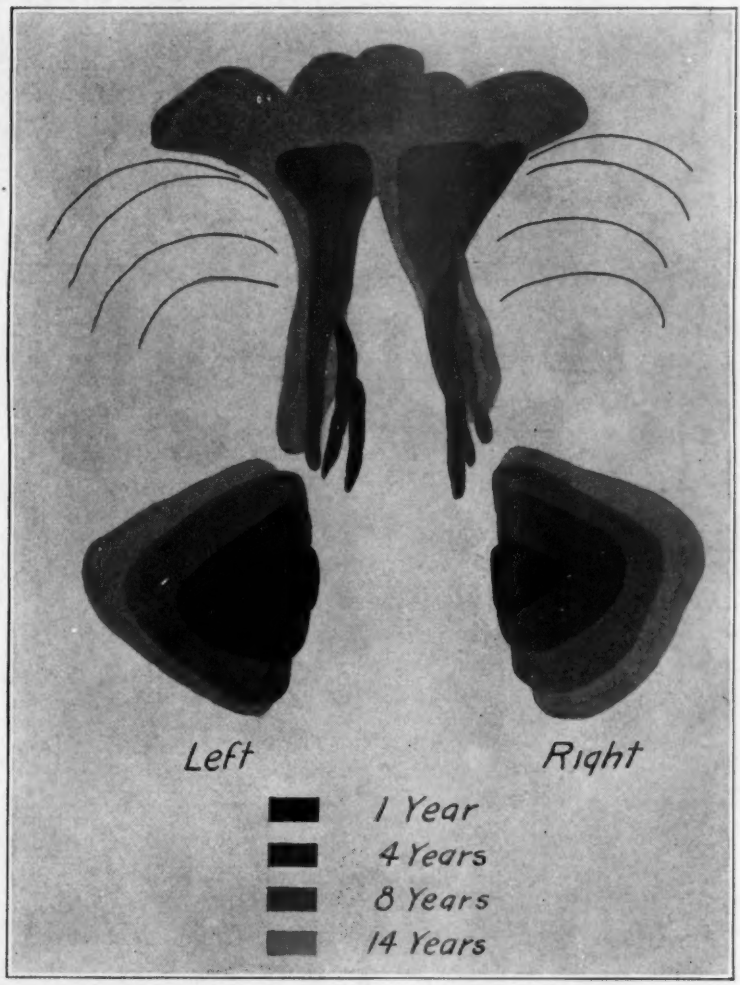

Fig. 13.—Composite drawing showing size and growth of the sinuses in J. S. (actual size of the tracings from the roentgenograms at each age represented).

regarded the frontal sinus as fully developed at 8 years of age. Haas [13] declared that he had never seen frontal sinuses before the age of 2½

16. Cited by Van Alyea, O. E.: Irrigation in Treatment of Disease of Frontal Sinus: Anatomic Clinical Study of Nasofrontal Connections, Arch. Otolaryng. **19:** 224 (Feb.) 1934.

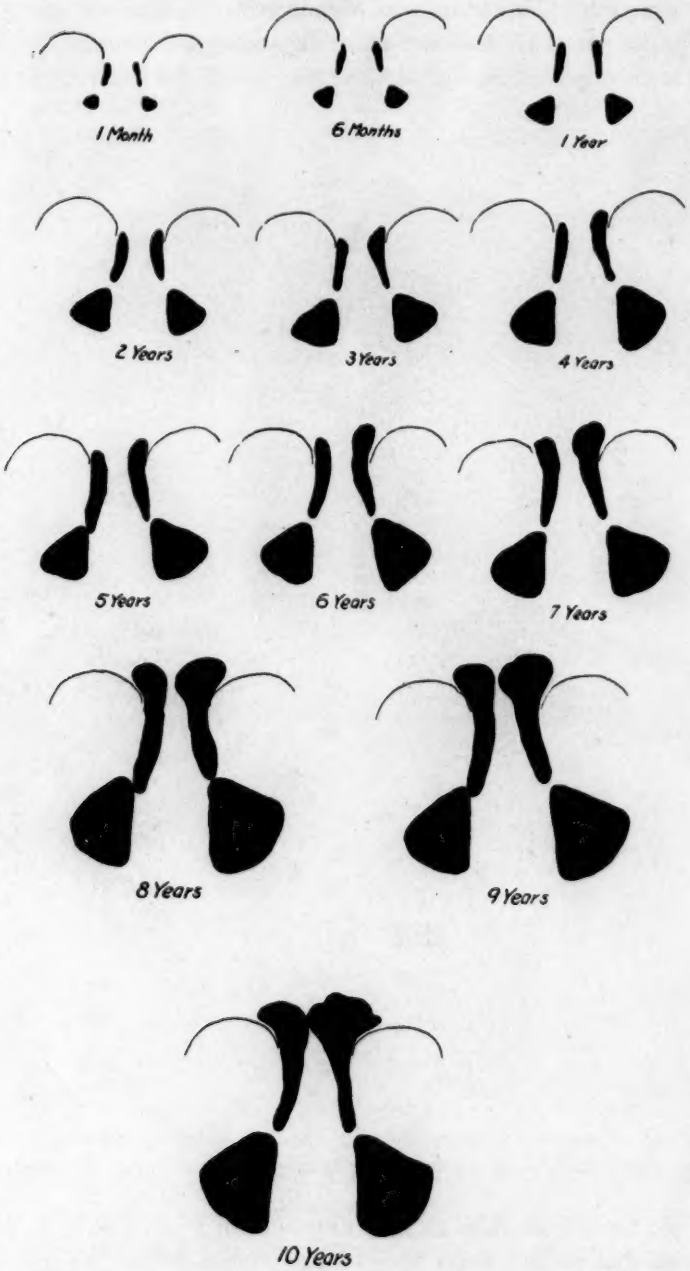

Fig. 14.—Drawing illustrating a sample series of all the tracings for one child (one-third actual size).

years, that they appear regularly from 4 years on but that children of 6 to 7 years of age without frontal sinuses are not rare.

The maxillary sinus is evident about the seventieth day of fetal life according to Schaeffer.[3] He stated that the ventrodorsal (length) measurement is always greatest and that up to the end of the third year the cephalocaudal (height) measurement is intermediate between the length and the mediolateral (width) measurement. During the sixth year the mediolateral measurement gains but seldom exceeds the cephalocaudal. By the end of the first year width has increased to extend

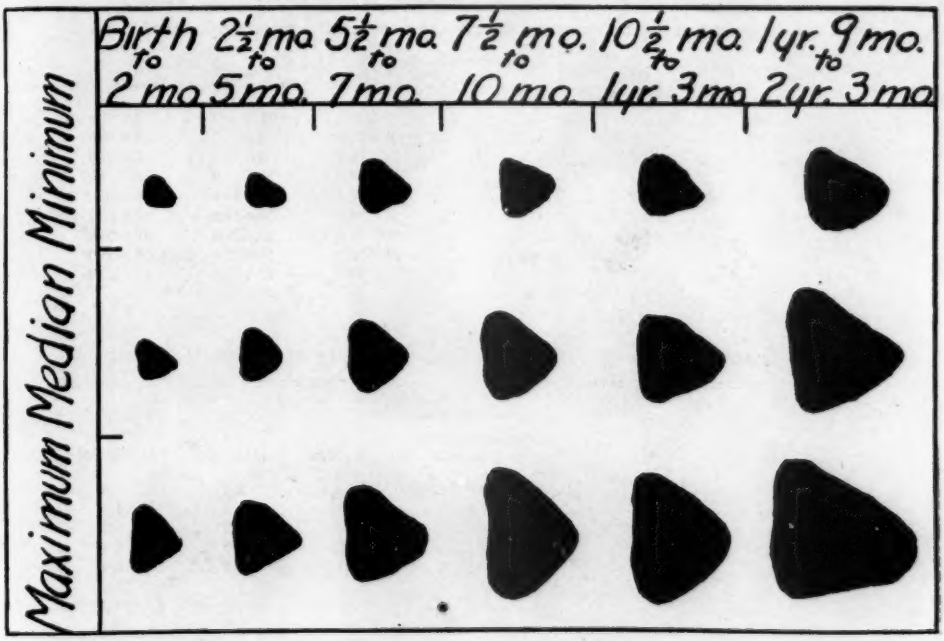

Fig. 15.—Range in size of antrums from birth to 2 years and 3 months.

beneath the orbit but not beyond the position of the infraorbital canal. At the twentieth month the sinus has elongated to 20 mm. in the ventrodorsal plane and has, as a rule, extended above the rudimentary first permanent molar tooth. During the third and fourth years the maxillary sinus makes a conspicuous growth in its mediolateral plane (width). By the seventh year the sinus measures on an average 27 mm. in length, 17 mm. in height and about 18 mm. in width. Schaeffer said that it is not true that large cavities always have thin walls or vice versa. In only 3 out of 20 subjects were the width measurements of the antrums of adults the same on the two sides. In 1 case there was 19 mm. difference between the two sides. He said he felt that in the adult age has no bearing on the size of the antrum and that sex affects size but slightly.

Warren Davis [14] said that the maxillary sinus increases in its diameters on an average of 2 mm. per year vertically and laterally and 3 mm. per year anteroposteriorly till the ninth year. From 9 to 15 years of age growth is slower, and the sinus is considered adult in type at 15 years. According to Sedwick,[17] the maxillary sinus reaches its greatest size during the third decade of life and does not increase in size thereafter. He also found great variation in shape, size and position of the sinus in different persons and in the sinuses on the two sides of the same person. Schaeffer's tables [18] representing size of the frontal and maxillary sinuses

TABLE 1.—*Schaeffer's Table for Average Size of Maxillary Sinus* [18]

	Maxillary Sinus		
Age	Length, Mm.	Height, Mm.	Width, Mm.
Newborn	7.0- 8.0	4.0- 6.0	3.0- 4.0
9 mo	11.0-14.0	5.0- 5.0	5.0- 5.5
1 yr	14.0-16.0	6.0- 6.5	5.0- 6.0
2 yr	21.0-22.0	10.0-11.0	8.0- 9.0
3 yr	22.0-23.0	11.0-12.0	9.0-10.0
6 yr	27.0-28.0	16.0-17.0	16.0-17.0
10 yr	30.0-31.0	17.5-18.0	19.0-20.0
15 yr	31.0-32.0	18.0-20.0	19.0-20.0
18 yr	31.0-33.0	20.0-21.0	19.0-21.0

TABLE 2.—*Schaeffer's Table for Average Size of Frontal Sinus*

	Frontal Sinus			
Age	Distance Above Nasion, Mm.	Height, Mm.	Width, Mm.	Length, Mm.
6-12 mo	2.0 (below)	2.0	2.0	3.5
1- 2 yr	1.8	5.0	2.5	4.5
3- 4 yr	2.5	7.0	4.0	5.5
7- 8 yr	9.5	13.0	10.0	8.5
10-11 yr	12.5	16.0	10.0	9.0
13-14 yr	12.0	16.0	9.5	10.0
17-18 yr	15.0	18.0	20.0	16.0
19-20 yr	28.0	26.0	26.0	17.0

illustrate, in a general way, the growth of the sinuses. Schaeffer said that since the frontal sinuses vary so greatly in size and shape and are usually asymmetric, any table showing growth is somewhat misleading.

The initial outpouchings of the ethmoid cells are evident as early as the fourth fetal month according to Schaeffer.[3] He gave the measurements of the anterior ethmoid group at birth as $5 \times 2 \times 2$ mm. and of the posterior ethmoid group as $5 \times 4 \times 2$ mm. He found the number of ethmoid cells to vary from 3 to 15. Davis [14] said that pneumatization of the lateral ethmoid mass proper is in the majority of cases complete at

17. Sedwick, H. J.: Am. J. Roentgenol. **32**:154, 1934.
18. Schaeffer, J. P.: Pennsylvania M. J. **39**:395, 1936.

birth. The cells subsequently increase in size not only by expansion but also by invasion of the surrounding areas, so that the distal boundaries may extend into regions such as the frontal region, the maxilla and the palate bone. In the adult the anterior group measure on the average 24× 23 × 11 mm. and the posterior group 21 × 21 × 12 mm.[15] Knutson [19] said that in the newborn infant the ethmoid portion of the nose

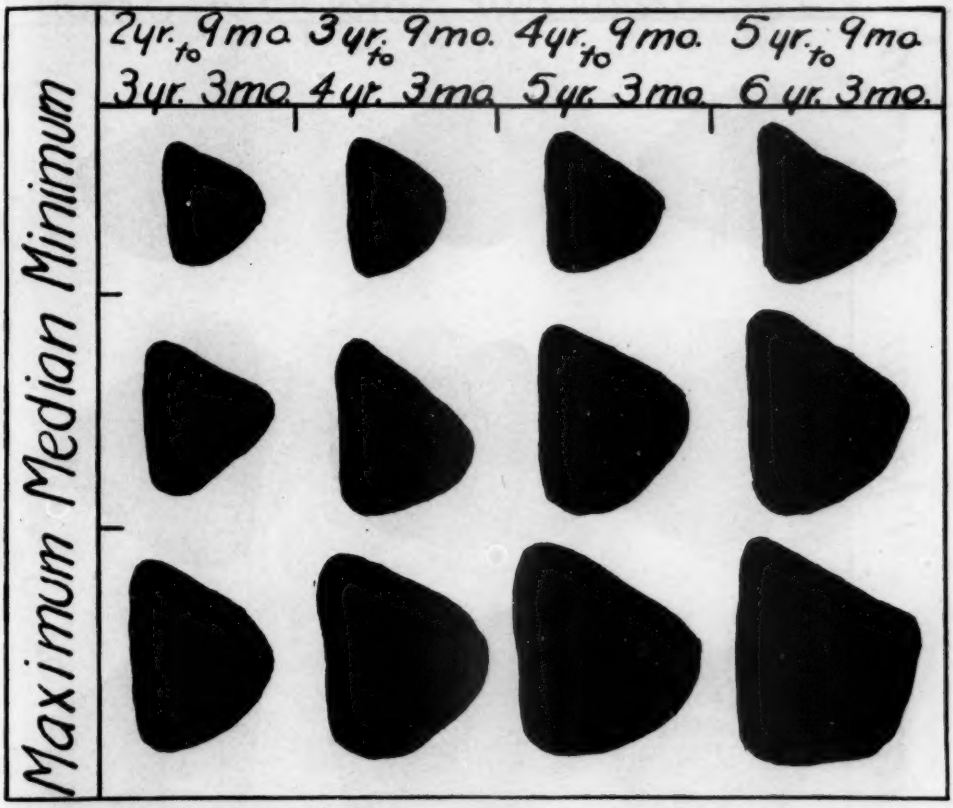

Fig. 16.—Range in size of antrums from 2 years and 9 months to 6 years and 3 months.

forms two thirds of the total height of the nasal cavities and the maxillary sinus one third. In the adult they are equally divided, for the maxillary sinus, growing more rapidly, attains its full height through growth downward while at the same time the choanae are increasing in height.

19. Knutson, F.: Nord. med. tidskr. **13**:606, 1937; cited by Salinger, S.: Paranasal Sinuses, Arch. Otolaryng. **28**:253 (Aug.) 1938.

MATERIAL AND METHOD

The roentgenograms from which the study was made were taken over a period of fourteen years on 100 children who are being examined from birth to maturity by the Child Research Council. Roentgenograms of the sinuses have been taken at

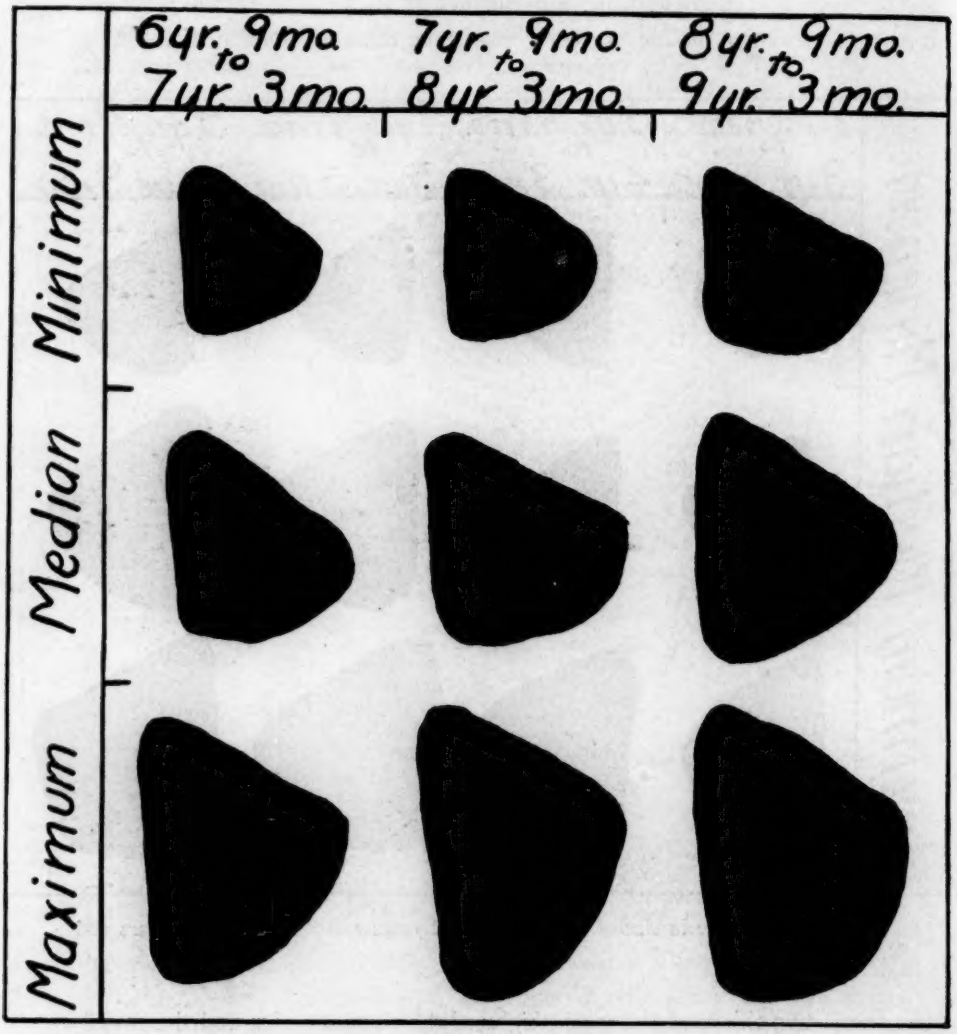

Fig. 17.—Range in size of antrums from 6 years and 9 months to 9 years and 3 months.

periodic intervals since birth for most of these children. Since no roentgenograms of the sinuses were taken here before 1925, the series for a few of the older children began at 3 or 4 years of age. The roentgenograms were taken on a 23 degree angle board with the nose and forehead in contact with the casette and with the roentgen ray tube directed straight downward. The focal film

distance was 28 inches at the center of the casette. No modifications of position have been made since this work was begun. For the older children other views have been taken for a number of years, but they will not be discussed or

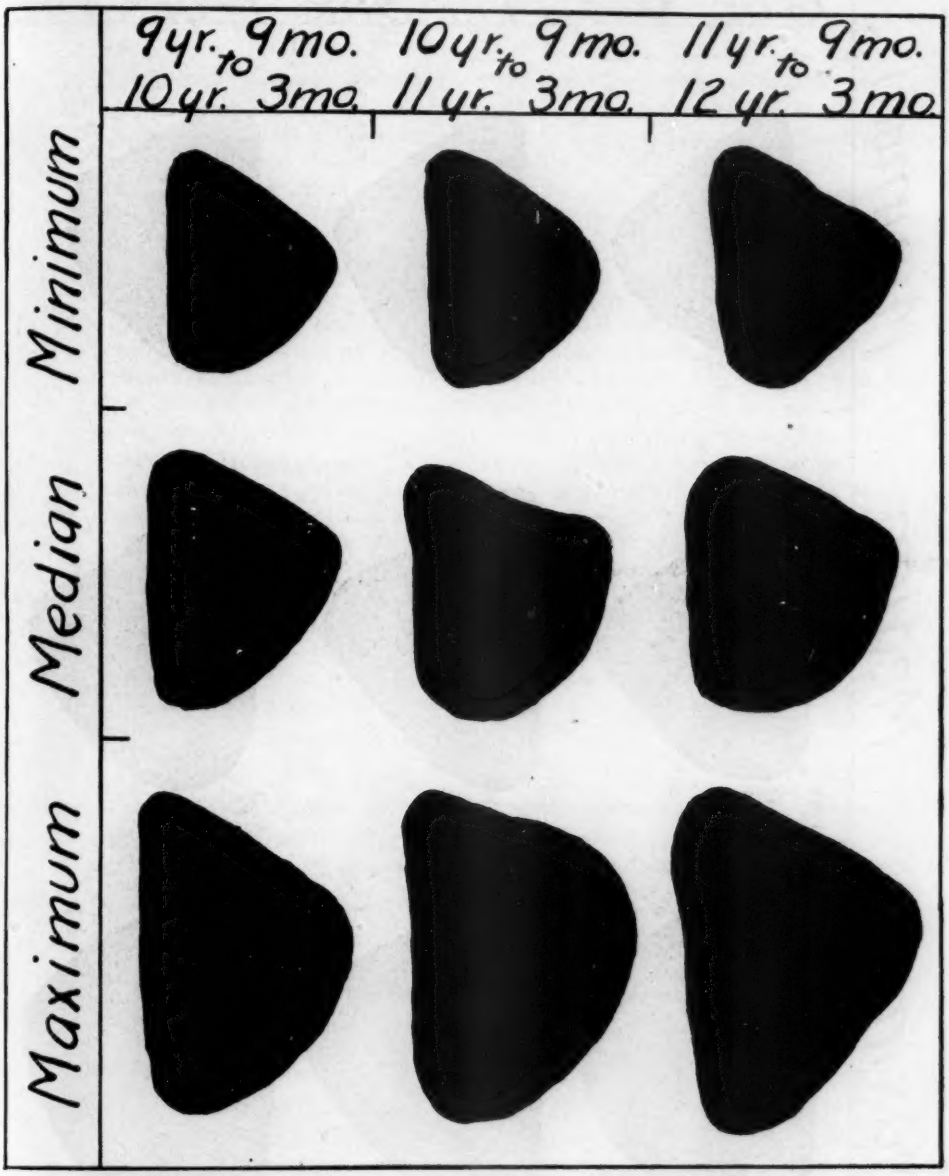

Fig. 18.—Range in size of antrums from 9 years and 9 months to 12 years and 3 months.

used in this study, since the size of the sinuses differs from that in other views. Obviously, the sinuses are distorted and magnified in this type of routine film and cannot be compared with size measurements reported from anatomic material.

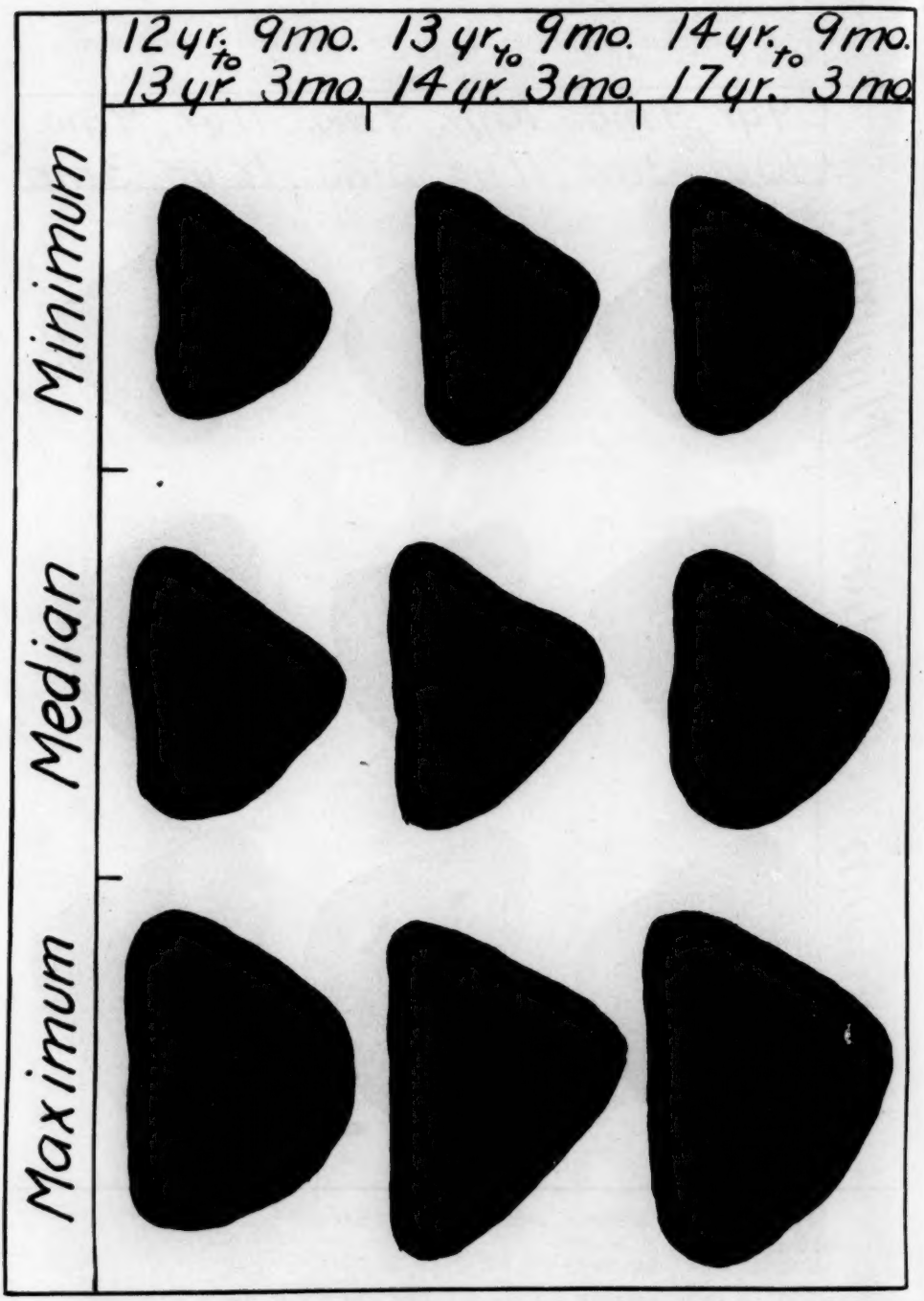

Fig. 19.—Range in size of antrums from 12 years and 9 months to 17 years and 3 months.

However, since roentgenograms are taken so frequently in medical practice, the sinuses on our routine films should not differ greatly in size from those taken elsewhere in the same position.

At the time this study was undertaken the series of roentgenograms of the 100 children covered different lengths of time. The youngest children had been followed up to 5 years of age. The oldest child had been followed to 17 years of age. There were 42 girls and 58 boys. Three children were 5 years old, 8 were 6 years old, 24 were 7 years old, 10 were 8 years old, 9 were 9 years old, 8 were 10 years old, 8 were 11 years old, 7 were 12 years old, 2 were 13 years old, 10 were 14 years old, 5 were 15 years old, 5 were 16 years old and 1 was 17 years old. All the roentgenograms of the sinuses taken from birth to the present age of each child were examined. Since actual measurements of the sinuses vary on the roentgenograms according to the shape of the sinuses and the level at which the measurements were taken, it was decided to study the size of the sinuses from tracings rather than from the original roentgenograms. These tracings were made with firm, transparent tracing paper (K & E Ionic. Light 197A) and fine pen on a horizontal viewbox which provided strong enough light to penetrate both the roentgenogram and the tracing paper. Tracings were made of each roentgenogram taken during the first year of life and once a year thereafter for each child. Frequently the sinuses could not be clearly outlined on a roentgenogram because of pathologic-appearing sinuses. In such a case a tracing was made of the preceding or of the succeeding film. If this was unsatisfactory no tracing was made for that year. The orbital roofs were traced as an orientation point. The ethmoid and frontal cells and the borders of the maxillary sinuses were then outlined on each tracing sheet. There is undoubtedly some error in tracing the borders of the sinuses in this manner, particularly along the nasal borders of the antrums and ethmoid cells, just as there is error in measuring sinuses directly from the roentgenograms. However, it was found that it was possible to produce nearly identical tracings from the same roentgenograms at different times, so this error was not considered significant enough to interfere with the results.

COMMENT

Many variations of size and shape of antrums, ethmoid cells and frontal sinuses were observed. In almost every case, growth was a fairly uniform process as it concerned the antrums and ethmoid cells. The antrums sometimes appeared asymmetric in both shape and size but the difference in size was usually not marked. The ethmoid sinuses appeared symmetric in almost every case.

Since the frontal sinuses are ethmoid in topography before they are frontal, it sometimes became difficult to distinguish on the roentgenogram exactly when a frontal sinus was developing. When the cells began to increase in size and appeared above the nasion I called them "budding frontal sinus cells." When the cupola of the frontal sinus had reached the level of the orbital roofs it was called a "true frontal sinus." These terms are purely arbitrary and are in a sense misleading, since a sinus can be a fairly well developed frontal sinus and not have invaded the vertical portion of the frontal bone to a level high enough to be above the orbit in the roentgenogram taken in the nose-forehead position.

However, the nasion is an easily located point and serves as an adequate guide to the development of the frontal sinus as studied from the roentgenograms. The reader should bear in mind, however, that from an anatomic viewpoint, the developing frontal sinus cells are really frontal sinuses regardless of whether they have invaded the vertical portion of the frontal bone or whether development has taken place wholly in the horizontal, or orbital, portion.

The frontal sinuses on the two sides did not always begin to develop at the same time. Nor did one side consistently begin to develop before the other. The speed of their growth process was very irregular as compared with that of the antrums. In many instances a cell would begin to bud upward and after reaching a point definitely above the nasion would fail to increase in size in succeeding roentgenograms for some time. Later the cell might increase in size very rapidly and either equal the size of the other frontal sinus or even become larger in a comparatively short time. There was no significant sex difference in time of appearance of the budding frontal sinus. The average age at which either frontal sinus was definitely evident above the level of the nasion and at which it began to increase in size was calculated as 3 years, although this is a difficult evaluation to make and might be interpreted differently by other examiners. The beginning frontal sinus was clearly seen in some children at between 1 and 2 years of age, and in a few instances there was no evidence of a frontal sinus developing before 6 to 8 years of age.

Since the children were not of the same age and had therefore been followed for varying numbers of years, it was not possible to obtain an average time for the appearance of the "true frontal sinuses," as I have called those cells whose cupolas are level with, or above the level of, the orbital roofs. And since the development of the two frontal sinuses was rarely equal, the data have been arranged in terms of the first frontal sinus to reach the level of the orbital roofs. Figure 1 shows the number of children who were examined up to the indicated ages. Since this is a longitudinal analysis, obviously all the children are in the 4 and 5 year age groups. Likewise the last age group represents only the 23 of the 100 children who have been followed continuously for thirteen years or longer. Figure 2 shows the percentage of children in each of the age groups just mentioned who had one or both frontal sinuses at the indicated ages. These percentages do not show the age at which the frontal sinus first reached the level of the orbital roofs. This age is shown graphically in figure 3, in which the data were regrouped according to the earliest roentgenogram which showed a "true frontal sinus."

Although the number of cases is too small for precise statistical determinations, the wide range of time over which frontal sinuses

develop is clearly demonstrated. The distribution in figure 3 is essentially that of normal expectancy and appears to indicate that the average time of appearance of frontal sinuses in the roentgenograms (at the level of the orbital roofs) is between 7 and 9 years of age.

No size measurements or groupings were attempted on the frontal sinuses because of the asymmetries and different shapes. Figures 4 through 13 show some of the different types of frontal sinuses observed.

When the tracings made from the roentgenograms of each child were superimposed with the centers of the antrums on the same horizontal plane the growth of the sinuses was strikingly demonstrated. In addition to frontal sinus growth already mentioned, the different types

TABLE 3.—*Number of Tracings from Roentgenograms of the Sinuses in Each Age Group**

Age Group	Number of Tracings
Birth-2 mo.	52
2½ mo.- 5 mo.	56
5½ mo.- 7 mo.	55
7½ mo.-10 mo.	60
10½ mo.-1 yr. 3 mo.	73
1 yr. 9 mo.- 2 yr. 3 mo.	82
2 yr. 9 mo.- 3 yr. 3 mo.	94
3 yr. 9 mo.- 4 yr. 3 mo.	97
4 yr. 9 mo.- 5 yr. 3 mo.	99
5 yr. 9 mo.- 6 yr. 3 mo.	96
6 yr. 9 mo.- 7 yr. 3 mo.	87
7 yr. 9 mo.- 8 yr. 3 mo.	65
8 yr. 9 mo.- 9 yr. 3 mo.	55
9 yr. 9 mo.-10 yr. 3 mo.	46
10 yr. 9 mo.-11 yr. 3 mo.	37
11 yr. 9 mo.-12 yr. 3 mo.	26
12 yr. 9 mo.-13 yr. 3 mo.	22
13 yr. 9 mo.-14 yr. 3 mo.	20
14 yr. 9 mo.-17 yr. 3 mo.	11

* Each age group contains only one tracing from each child in that group, so that the "number of tracings" also represents the number of children in each group.

and sizes of antrums, as well as the rate of growth of the sinuses, are easily seen. Figures 4 through 13 show (actual size) representative samples of these tracings; only a few of the tracings for each child are used, in order to simplify the illustration. (It is interesting to note that the child represented in figure 12 is the fraternal twin of the one represented in figure 13). A sample series of all the tracings for 1 child is shown (one-third actual size) in figure 14. Such longitudinal studies of the growth of the sinuses in individual children appear to illustrate better than measurements the futility of trying to establish a single "norm" representing either the size or the shape of the sinuses at any given age.

When all the tracings for each child were separated and arranged into age groups, the variations in size of the antrums were even more obvious. The number of tracings in each age group are given in table 3.

As I have stated before, the right and left antrums were not always identical as to size. Since in most instances the difference in size was slight, the larger of the two antrums of each tracing was chosen arbitrarily as the significant antrum for comparing the relative size in different children of the same age. Then the tracings were arranged in order from the smallest to the largest antrums in each age group. It was interesting to observe that each child maintained a fairly constant position in the total group when the yearly tracings were arranged in order of size. That is, the children with the smallest antrums in one age group would also have the smallest antrums in the following age groups. Likewise the same children were always in the upper 10 per cent of the group and had the largest antrums at each age level. Figures 15 through 19 show the total range in size of the antrums in each age group—maximum, minimum and median. These are presented actual size, although again the reader must realize that they are not to be construed as representing the anatomic size of the antrum. They are, however, the size of the sinuses as traced from our routine roentgenograms and should serve for comparison with other standard films taken in the same position.

SUMMARY

Tracings were made from the routine roentgenograms of the sinuses of 100 children who are being followed from birth to maturity at the Child Research Council. The youngest children had been followed up to 5 years of age. The oldest child had been followed up to 17 years of age. Examinations have been continual, beginning during the first month of life in most cases. The growth of the sinuses in these children is discussed and illustrated; stress is laid on the variations in size and shape of the maxillary sinuses and the variations in time of development and in size of the frontal sinuses.

THYROTOXICOSIS

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SAN FRANCISCO

This study is the result of ten years' observation of 62 patients who have had thyrotoxicosis during the past twenty-five years. Nearly all the patients have been followed for nine years in conjunction with the thyroid committee of the university clinic. The hyperthyroidism was definitely marked and not mild. Neither the forme fruste, or latent type, nor the relatively transitory simple hypertrophy occurring at puberty is included. One of the accomplished purposes of the study was the observation of most of the patients some years after full arrest had occurred and of a few when the disease was still active. Thus, something of the natural course of the disease was determined, and the therapy was appraised. The number of cases is too small to prove the validity of the observations. For clarity, nevertheless, the following impressions are very likely.

NATURAL COURSE OF THE DISEASE

The onset of the disease may be as early as at the ages of 3 to 5 years; most commonly it occurs in early adolescence, at 12 to 14 years, and is arrested by the eighteenth year, with an occasional recurrence as late as the thirtieth year. Multiple cycles of the disease usually recur from two to four years before full arrest sets in, and from three to four cycles are common. Succeeding cycles usually become less severe and shorter. The relapse phase of a cycle may last from two months to several years and the remission phase from several months to several years. A child never has a total remission. This disease "waxes and wanes"; there is activity of some degree until full arrest, inactivity, occurs (see chart).

Fifty-five per cent of these patients required surgical care because toxicity was severe and persistent. Twenty-five per cent of all the patients had complications of the disease. It might be deduced that in half of the cases thyroid hyperplasia is relatively benign, self limited, short lived and not a great menace to health in childhood or in later life. However, such toxicity was often serious, even though surgical inter-

From the Department of Pediatrics, the University of California Medical School.

Read at the annual meeting of The Society for Pediatric Research, Skytop, Pa., April 26, 1939.

vention was not required. Also, in some cases toxicity recurred in later years, and definite complications ensued requiring surgical treatment to arrest cardiac disease, disturbances of the nervous system and difficulties during pregnancy.

ETIOLOGY

Familial occurrence of this disease, overactivity of the parasympathetic nervous system, infection and adolescence with its accompanying "hyperpituitarism" and emotional upsets, singularly or more often in combination, brought on the disease. In at least 8 instances the disease had occurred in others in the family, either in the same or in previous generations. No patient had true hyperventilation. While infection was a strong factor in many, other agents were effective. The role of sex and adolescence and, according to my observations, the probable overactivity of the anterior lobe of the pituitary are striking factors. Later, the pituitary factor will be discussed in detail.

SIGNS AND SYMPTOMS

The clinical picture in children is the same as that occurring in adults, with several exceptions. These are in skeletal growth and

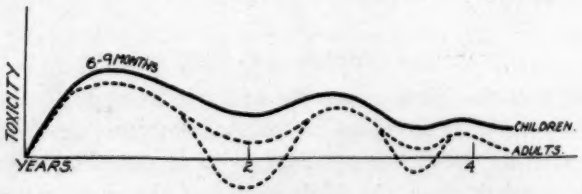

Chart showing approximately the natural course of thyrotoxicosis as observed in ten years' study of 62 patients who have had thyrotoxicosis during the past twenty-five years.

in sexual maturation. There were 8 boys and 54 girls, a ratio of 1 to 6.75. The age of the onset of toxicity was between early infancy and 5 years in 5 patients, between 6 and 10 years in 19 patients and between 11 and 15 years (mainly between 13 and 15 years) in 28. All the patients were brought up in California except for a Polynesian, whose condition developed in Tahiti. The mountainous areas of California are endemic for this disease, and toxicity developed in many of the patients there. The onset of the disease occurred, however, in about a third of the patients while they were in the valley areas. The occurrence of the disease may be linked with a low intake of iodine in the water. The disease developed in 8 patients in San Francisco, not a low iodine area. The nationality of the patients was as follows: 1 Chinese, 1 Polynesian, 52 northern Europeans, 1 Russian and 7 southern Europeans.

Information on skeletal growth was available for 44 patients. Thirty-six were tall, and 8 were of average height. It was noted that statural growth was often rapid before the onset of toxicity and that this disease came on frequently just before puberty or at other times of growth spurts. Parallel with this "gigantism," the epiphysial age was accelerated markedly. Girls of 13 and 14 years of age often had bone ages of 16 to 18 years. Tall girls were often eunuchoid in proportion, but occasionally they were heavy framed and "acromegaloid." The more active the disease and the longer its duration the greater the resultant "gigantism" and likewise the acceleration of epiphysial age.

The teeth, a skeletal appendage, often are prematurely developed and erupted, depending directly on the severity and duration of the activity.

Calcium and phosphorus balance studies indicated demineralization of the body and skeleton (and possibly about the apexes of the teeth) varying directly with the duration and severity of the activity. The usual excretory channels (70 per cent urine and 30 per cent bowel) transported this loss in the calcium content.

Information on sexual maturity was available for 31 girls. Thyrotoxicosis tends to suppress ovarian function. Often secondary sexual characteristics fail to appear during toxicity, or they develop only very slowly. Menstruation failed to develop in 4 and was scanty in 4, and amenorrhea followed toxicity in 9. However, the menses were normal in 15 during toxicity. In the only boy studied, sexual maturation was retarded. The more active the toxicity, the longer its duration and the nearer it occurred to expected puberty, the more suppressed was sexual maturation.

Since increased skeletal growth precedes symptoms of the disease and since the disease occurs more often during the normal periods of growth spurts, predominantly just before and during the growth of puberty, hyperpituitarism and thyrotropic hormone may play an activating part.

This study does not include borderline cases. Diagnosis in such instances is often difficult and requires time, and the condition may prove to be mainly vasomotor instability or finally hyperventilation with secondary overactivity of thyroid function. The truly toxic patients complained of nervousness, excess perspiration, loss of weight, tremor, tachycardia, exophthalmos and struma with thrill and bruit. There was little gastrointestinal disturbance. The basal metabolic rate was used to confirm the clinical impression and did not rule it in or out. I do not feel that the rate can be relied on too often to determine the presence or absence of the disease, or that it can always be relied on to gage its severity.

THERAPY

The proper therapeutic procedure is a much debated and unsettled source of contention, especially for the decade and a half of child life. There have been many strikingly fine results attained in different parts of the world by medical, surgical or radiation procedures. In the past ten years a definite approved plan has been carried out for all patients. Naturally changes occur which influence the efficiency of a previously planned therapeutic procedure. Again, the worthiness of certain procedures from 1914 to 1929 may be questioned, since during that period between the onset of the disease in the first recorded case, and the establishment of the thyroid committee the therapy was not controlled by a plan of the thyroid committee. Finally, one must remember that it is the natural course of exophthalmic goiter to have relapses and remissions and perhaps to cease spontaneously. It is felt that this report carries a follow-up sufficiently long after therapy was completed to appraise properly the efficiency of such therapy and its relation to the natural course of the disease. In previous studies, such a protracted follow-up has only rarely been carried out.

An attempt has been made to separate the influence of compound solution of iodine U. S. P. from that of rest in bed, sedation and other agencies in medical therapy. Furthermore, a differentiation has been attempted between resulting improvement and arrest of the disease and not merely the remissive stage of a toxic cycle. The word "cure" has been diligently avoided and "arrest" substituted, because reactivation of toxicity may occur years later in adult life.

The influence of medical therapy will be considered first. An examination of table 1 reveals that rest in bed was the reason for the arrest of toxicity in only 3 patients. These patients were ill for one year before; 1 was treated for three and one-half years. Compound solution of iodine U. S. P. arrested toxicity in 4 and improved 2; the disease was not active too long previously; the administration of the iodine did not require too much time, and the condition of each patient has been followed up for an average of nearly eight years. Another group required both the iodine solution and rest in bed. Occasionally the disease was more active and of longer duration in the latter group. The arrest of activity has been permanent, as judged by an average follow-up of seven years. In the past decade most of these patients have been given 1 to 5 drops of compound solution of iodine U. S. P. daily, since it was believed that the effects, as judged by present clinical checks, were as good as might be obtained with 15 to 30 drops. Higher doses such as these were given preoperatively.

Some of the 15 patients receiving medical treatment did not have the most severe or malignant type of thyrotoxicosis; yet most had exophthalmic goiter and surgical treatment would have been justified.

Since it was not resorted to, follow-up observation shows how closely the course of the disease in many of these patients fits into the natural course of the disease. Two patients distinctly represent this, and therapy was not influential since it was not well carried out. The disease in these cases was probably spontaneously arrested. Medical regimen arrests toxicity in cases of mild forme fruste but effects similar results in only about half of the cases of more severe grades of toxicity. However, complications and sequelae are lessened during medical treatment. There were 15 other patients for whom medical therapy failed and roentgen or usually surgical treatment was necessary. To repeat a previous statement—about half of the patients required surgical treatment for severe toxicity.

TABLE 1.—*Results of Medical Treatment of Thirty Patients* *

Treatment	Result	Number of Patients	Duration of Disease, Months	Duration of Therapy, Months	Follow-Up, Years
Rest in bed	Arrest	3	12	6	6
			12	42	6
			12	2	7
Compound solution of iodine U. S. P.	Arrest	4	12	3	5
			12	2	4
			24	1	4
			12	6	7
	Improvement	2	12	4	8
			6	6	4
Compound solution of iodine U. S. P. and rest in bed	Arrest	5	1	3	4
			12	6	13
			48	48	12
			36	6	1
			6	6	13
	Improvement	1	6	3	4

* The table includes data on the 15 patients who received medical treatment only; the treatment of the remaining 15 required surgical and roentgen treatment.

Severe exophthalmic goiter rarely shows more than temporary improvement during the prolonged use of iodine. A mildly active disease may naturally become more severe while iodine is being used. The response depends rather on what is happening spontaneously to the disease than on the administration of iodine. In patients showing satisfactory results, iodine may only slightly check the toxicity, while the disease pursues its natural course toward remission or even spontaneous arrest. This helps even in mild exophthalmic goiter.

A one stage radical removal of the thyroid gland (90 per cent) arrested the disease in over 90 per cent of the patients. Occasionally (in 4 patients) roentgen therapy was used immediately after surgical removal, for further insurance. One recurrence took place as long as nine years postoperatively and was successfully arrested by irradiation.

Of the 3 patients requiring a second operation, 1 was inadequately operated on elsewhere. This amounts to a surgical recurrence of 6 per cent in this clinic. Only 1 patient, whose condition was not counted as a recurrence, was treated preoperatively by ligation, as this was the only advisable and safe procedure.

Preoperative roentgen therapy was not so successful in reducing the activity of the thyroid gland. The dosage varied over the years and may have been inadequate. Radium helped in 2 cases.

Before surgical arrest, 28 of the 33 patients operated on were treated by other means. Medical therapy (with iodine solutions) was inadequate for 7 of 11 patients but helped all. Compound solution of iodine U. S. P.

TABLE 2.—*Results of Surgical Treatment of Thirty-Three Patients*

	Number of Patients	Arrest	Nonarrest; Also Recurrence	Average Years Followed
Patients having 1 operation	30	30	2†	6 plus
Patients having 2 operations	3*	2	1	

* The condition of 1 patient, arrested surgically at 11 years, required irradiation at 16 and 18 years and a second operation at 19 years. The case has been followed 7 years since. A second patient was reoperated on after 4 months; a third was reoperated on after 6 months and 2½ years later required roentgen treatment.

† Radiation arrested recurrence in 1 patient 9 years postoperatively.

TABLE 3.—*Therapy Before Surgical Arrest*

	Medical Regimen: Rest, Sedation, Compound Solution of Iodine U. S. P.	Preoperative: Compound Solution of Iodine U. S. P.	Roentgen Therapy	One Operation
Inadequate	7	0	3	3
Adequate	4	26	5 (2 radium)	

always aided when properly given preoperatively. Roentgen treatment improved 5 but failed to help 3. A single operation, as previously explained, failed to arrest activity in 2 patients. All 28 patients had to be operated on, since no other therapy arrested the disease.

In the treatment of extremely severe exophthalmic goiter in children, surgical intervention has offered the most aid for arresting toxicity. Other methods often only temporize; however, they may help to prepare for safer and more "curative" surgery. Nevertheless, surgical intervention may be only palliative for some children, since it does not always remove the cause of such overactivity of the thyroid gland.

Roentgen therapy was mainly a supplement to surgical treatment. It has helped preoperatively and has been almost specific for surgical recurrence if it is not too severe or if it is given not too long postoper-

atively. It was well controlled in the case of 4 patients, curing 3 and improving 1. However, roentgen therapy may prove to be valuable in the future, for inducing both early remissions and arrest. Radium, as bare emanation tubes, was successfully used preoperatively for 2 patients.

TABLE 4.—*Patients Receiving Roentgen Therapy With or Without Other Medical Care and Without Surgical Treatment*

Date	Amount	Compound Solution of Iodine U. S. P.	Medical Care	Result	Duration in Months Before Roentgen Therapy	Follow-Up, in Years
1934	975 r	For 4 months before	Before and after	Improvement	4	3
1935	2,700 r	Before	Before and during	Arrest	9	3
1930	? 800 to 1,000 r	None	None	Arrest	42	9
1922	4.5 mc. radium	.....	Before	Arrest	0	17
1934	1,200 r	For 1 month before	.....	Arrest	6	5

The following tabulation shows the agreement or the lack of it between preoperative and pathologic diagnoses.

Clinical Diagnosis	Hyperplasia with Adenoma		Thyroiditis		Malignant Growth	
62 patients	62		13	4	1	
33 surgical patients	29 1 colloid		8	1	1	
Pathologic diagnosis of 33 surgical patients	Yes 32	No 1	Yes No 4 4	Yes No 3 1	Yes 1	No ..

Follow-up examination has been made personally of 49 of the 62 patients whose records were studied. Contact with the remainder has been made by mailing questionnaires.

RECURRENCES

Following the medical, surgical and roentgen therapy there were 12 definite recurrences and 3 questionable ones. Definite recurrences may occur in adult life, even ten to twelve years after successful arrest of the disease. Of the 12 definite recurrences, 6 occurred in patients between the ages of 18 and 30 years (the oldest observed in the follow-up). There had been lapses of three to twelve years since the previous activity. Most of these patients were previously treated by medical means, and some were treated by a very radical surgical procedure. Surgical recurrence occurred in 6 per cent of the patients, 5 to 10 per cent being a permissible figure. Surgical treatment is not always curative, as many surgeons will admit. Among some of the women,

ovarian deficiency in menstruation, sterility and spontaneous abortion seemed to be related to their having exophthalmic goiter in childhood.

COMPLICATIONS

The presence or absence of complications was noted in the records of 51 of the 62 patients. Complications occurred in 12 of the 51 patients. Those referable to the active disease will be considered first. Mild hypothyroidism occurred once after six years of very active toxicity. The exophthalmic goiter was sporadically treated and probably was uninfluenced by therapy.

Myocarditis was encountered in 7 patients, and all recovered. Fibrillation occurred once. Osteoporosis was observed in 3 patients, and in 2 it was mild. Alopecia was seen in 1 patient, and eunuchoidism in 2 patients. Nervousness was frequent. Thyroid crisis occurred in 2 patients.

Among the 33 patients who were operated on, complications were as follows: Hypothyroidism was permanent in 2 patients. One patient had a resection of a small amount at 14 years, after one year of mild disease, and had a mild deficiency four years postoperatively. The other patient had four fifths resected at 11 years for severe symptoms three months after the onset; twelve years later she had a marked deficiency, although a recent illness with pneumonia may have aggravated this.

A third girl had marked toxicity for two years, 7 Gm. of the goiter being resected at 8 years of age. There was no other previous therapy; at 12 years a mild hypothyroidism began and was still present at 30 years. This may have been due to puberty rather than to surgical treatment.

In 4 instances hypothyroidism after operation was temporary. There were probably other such instances. In these cases the disorder was mild and required ½ to 2 grains (0.03 to 0.13 Gm.) daily of desiccated thyroid for six months to one year. Such hypothyroidism is desirable, as the slight postoperative deficiency produced by radical removal is compensated by the cause of the disease, which induces hyperplasia in the remaining thyroid to about a normal amount or to a slightly greater amount of tissue.

In 2 patients hypoparathyroidism was permanent but mild, and the symptoms were controllable. In 2 it was temporary, but mild. In 1 patient it lasted nine years, and hyperventilation was present.

Neither paralysis nor injury of the larynx occurred, nor were there postoperative hemorrhages, mediastinitis or deaths.

EFFECTS IN ADULT LIFE

The adults observed often were tall and occasionally had heavy, wide skeletons. These influences on growth varied with the severity and

duration of the disease in childhood. The greater the duration and the nearer the duration to the time of full skeletal growth, the greater was the height. Tallness plus a heavy skeleton indicate overactivity of the pituitary growth factor. While menstruation may have been disturbed, resulting in such complications as delayed menarche and oligorea during the activity, it usually was uninfluenced in adult life. It was questionable whether sterility and failure to carry a child until term could be related to exophthalmic disease in childhood or to reactivation of the disease later. The other complications and sequelae were not influential in adult life. If well treated during childhood and adolescence, the disease usually stopped by the eighteenth year; however, there were exceptions.

Case Reports

AMAUROTIC FAMILY IDIOCY

STUDY OF A CASE OF THE LATE INFANTILE TYPE

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At the present time three types of amaurotic family idiocy are generally recognized: the infantile, with onset of the disease under 1 year; the juvenile, with onset between 6 and 14 years, and the late form, occurring in adult life. In addition, a few cases have been reported with age incidence between 1 and 5 years and termed, accordingly, "late infantile" cases. Features such as the protracted course, the absence of macular changes and the occurrence of cerebellar atrophy have been considered characteristic of this type.

The present study reports a new case of "late infantile" amaurotic idiocy. The clinical report may be of interest because of the extreme enlargement of the head. The pathologic examination showed certain unusual features that bring to the fore the question of the relationship of amaurotic idiocy to familial diffuse sclerosis. Moreover, special attention was directed to the investigation of the chemical nature of the lipoid content of the nerve cells in the attempt to contribute to the solution of the controversial problem concerning the nature of the disease.

REPORT OF CASE

H. C., a white boy aged 3 years and 4 months, was admitted to Letchworth Village on Dec. 7, 1937. The family history was not contributory. The patient had one normal sister, aged 6. The parents, of German-Hebrew stock, were healthy. There was no consanguinity.

The early history was irrelevant; development had been apparently normal until the age of approximately 1½ years, when it was first noted that the patient showed signs of mental backwardness. He could not sit up as before, failed to smile, and no longer reached for his food or took notice of his surroundings. At the same time, his head seemed to become larger. Mental defectiveness became gradually more pronounced; at 2 years of age the patient was classified as a low grade idiot. The size of the head increased progressively until at 2 years it reached huge proportions. A diagnosis of hydrocephalus was then made by physicians. Convulsions were observed for the first time at 18 months and became more and more frequent until almost continuous status epilepticus was observed at the age of 3 years. At the second year of age, blindness became apparent.

Physical examination on admission showed a well developed boy. The head was strikingly enlarged, the anteroposterior diameter being 8 inches (20 cm.)

From the Research Department, Letchworth Village, Thiells, N. Y.

and the transverse diameter 4.75 inches (12 cm.) The enlargement was symmetric. The fontanelles were closed. The head was held in extension; the usual posture of the limbs was also in extension, at times with flexed hands. There was a general increase of muscular tone. The deep reflexes were markedly hyperactive, and bilateral clonus of the rotula and foot was elicited. Babinski's sign was present on both sides. Stroking of the abdomen produced a sudden hyperextension of the limbs and contraction of the abdominal muscles. Stroking the palmar surface of the hand elicited a clench that lasted for over one minute. Champing movements of the lips were induced by any stimuli on the lips. Pricking the dorsal surface of the feet produced a slow flexion of the legs. The pupils were dilated and reacted sluggishly to light. The eyeballs were in slow continual rhythmic rotating movement. Lateral nystagmus was occasionally observed. Both optic disks were markedly atrophic, but the macula lutea was normal in both eyes.

The patient was completely deficient mentally, taking no notice of his surroundings.

The cerebrospinal fluid was normal in all respects.

A roentgenogram of the skull showed diffuse thinning of the bones besides the symmetric enlargement already referred to.

No important changes were noted during the patient's residence in the hospital. Death occurred on Dec. 22, 1937, following bronchopneumonia.

Pathologic Examination.—The autopsy was performed twelve hours after death.

The brain was much larger than normal and weighed 1,980 Gm. The leptomeninges were thickened and cloudy but not adherent to the cortex. The gyri were decidedly widened. The main sulci and convolutions could be easily identified, but accessory folds and fissures were scanty. The optic nerves appeared atrophied. The cortex was thicker than normal, and showed a peculiar rubber-like consistency, whereas the white matter appeared soft and gelatinous throughout. The limits between gray and white matter were sharply marked. There was no dilatation of the ventricles.

In striking contrast with the cerebral hemispheres, the cerebellum appeared small and sclerotic. The pons and medulla also appeared smaller than normal.

Histologic Examination.—The histologic study was made by the usual methods, including those of Van Gieson, Nissl and Bielschowsky for nerve cells; Weigert, Spielmeyer and Weil for myelin sheaths; Cajal, Hortega, Holzer, Anderson and Alzheimer VI for glia. The lipoids were studied with scarlet red, sudan III, osmic acid, nile blue and hematoxylin.

Nerve Cells: In Nissl preparations the neuron cells showed the characteristic alteration of amaurotic idiocy (fig. 1): The cells were swollen; the tigroid substance had disappeared; the nucleus was displaced, generally normal and only occasionally dark and shrunken or pale and swollen. Swelling of the dendrites was rarely seen. The cytoplasm was filled with finely granular substance that stained faintly pink with scarlet red, pale brown with osmic acid, black with hematoxylin, and pale blue with nile blue. The granules appeared to be readily dissolved in a mixture of chloroform and methyl alcohol (1:3), whereas a short immersion in cold alcohol, acetone or ether did not alter the staining property of the lipoid. By Hurst's [1] method, optimum staining of the cytoplasmic material was obtained after four days of mordanting in chromium solution. In Bielschowsky preparations the fibrillary network either had disappeared or was reduced to a

1. Hurst, E. W.: A Study of the Lipoids in Neuronic Degeneration and in Amaurotic Family Idiocy, Brain **48**:1, 1925.

cluster of fibrils located at the periphery of the cell. The neurofibrils in the dendrites were much better preserved. No intracellular argentophil bodies were detected. Occasionally, nerve cells were seen which appeared shrunken, with a few granules of lipoid and irregular dark Nissl bodies.

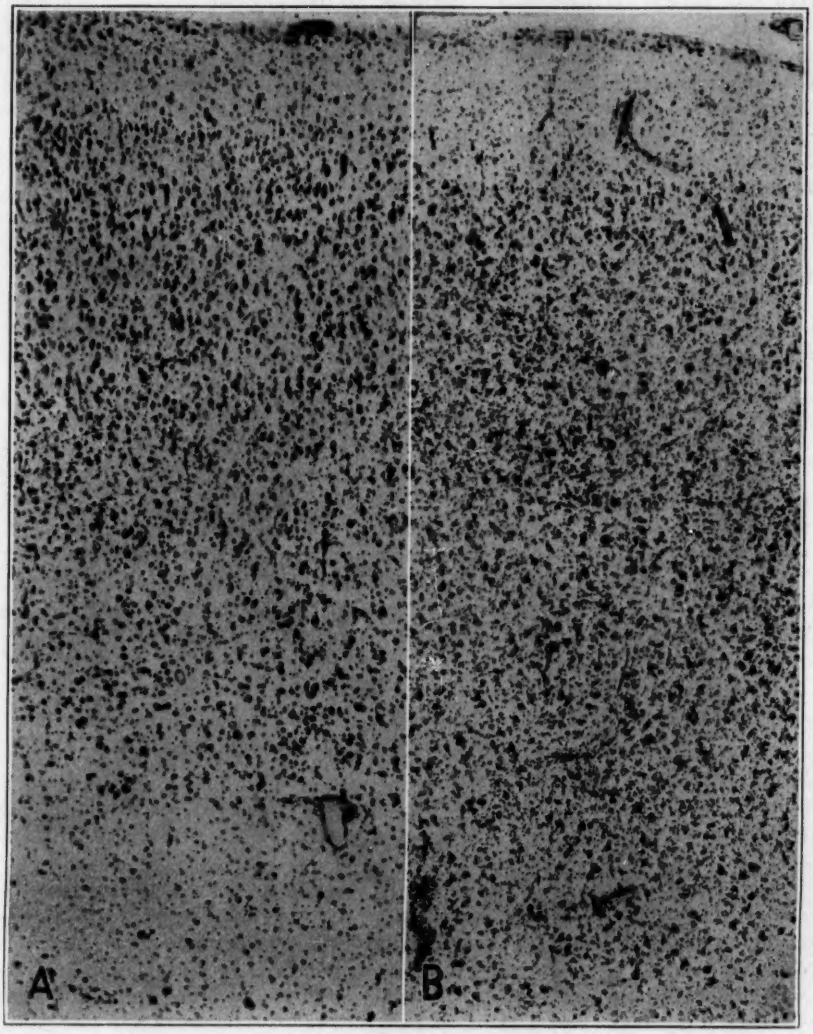

Fig. 1.—The frontal (*A*) and the parietal (*B*) cortex in the Nissl preparation (low power), showing the characteristic neurocellular swellings.

The cellular alteration extended to the whole cortex. Practically no neuron cell was normal. All laminas were equally involved. However, the normal cyto-architecture could be recognized fairly well, since apparently no considerable dropping out of nerve cells had occurred.

The nerve cells of basal ganglions, midbrain, pons, medulla and spinal cord presented the ballooned appearance characteristic of the disease (fig. 2). However, the cells of the substantia nigra, the pontile nuclei and the globus pallidus appeared less misshapen and infiltrated than the others. In every region the staining reactions were essentially the same.

Myelin: Weigert, Spielmeyer and Weil's method showed a striking alteration of the myelin sheaths. There was demyelination extending to the whole white matter of the brain. In no section was an area found in which the myelin stained normally. The subsulcine fibers were likewise involved. Large Weigert sections including the whole hemisphere (fig. 3) showed the extension of the demyelinating lesions. Contrasting with the paleness of the white matter in Weigert prepara-

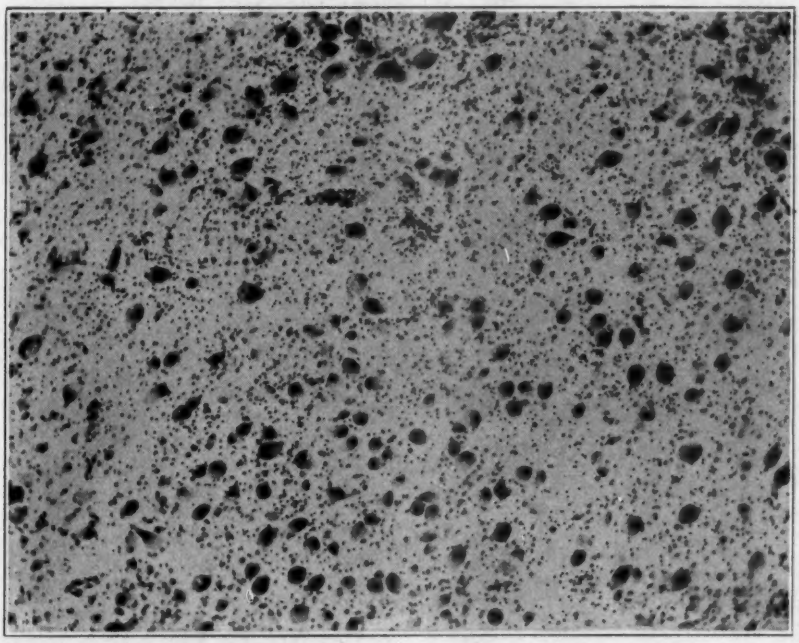

Fig. 2.—Corpus caudatum in the Nissl preparation (medium power), showing extensive neurocellular swellings.

tions was the dark color of the gray matter in which the intracellular lipoids were stained by the hematoxylin. In some portions of the centrum ovale a few faintly stained areas were observed, containing a vast number of granules, which stained palely with hematoxylin, and fragments of myelin sheaths. Occasionally, in better preserved regions the sheaths were decidedly reduced in number, appeared considerably thinner than normal and showed small, circumscribed swellings which gave a beadlike appearance to the myelin sheath.

Axons: In Bielschowsky preparations, the axis-cylinders appeared still present in areas of complete demyelination. However, they were decidedly reduced in number and showed pathologic alterations, such as irregularity of contour and corkscrew-like appearance.

Glia: The macroglia showed marked proliferation in the whole cortex. Plasmatic glia cells with numerous and long dendrites were seen in the various

cortical laminas, being particularly abundant in the molecular and in the sixth layer, where decided gliosis was demonstrable with Holzer's method. In the white matter the macroglia had undergone striking changes, which were most pronounced in the subcortical white matter. Here large protoplasmic cells were very numerous, at times collected in large clusters. The cytoplasm was often filled with granules exhibiting the same staining properties as those shown by the lipoids in the nerve cells, i. e., black with hematoxylin, pale rose with scarlet red and sudan III, pale brown with osmium. Numerous glia cells showed two and occasionally three or four nuclei (fig. 4). Some cells showed the

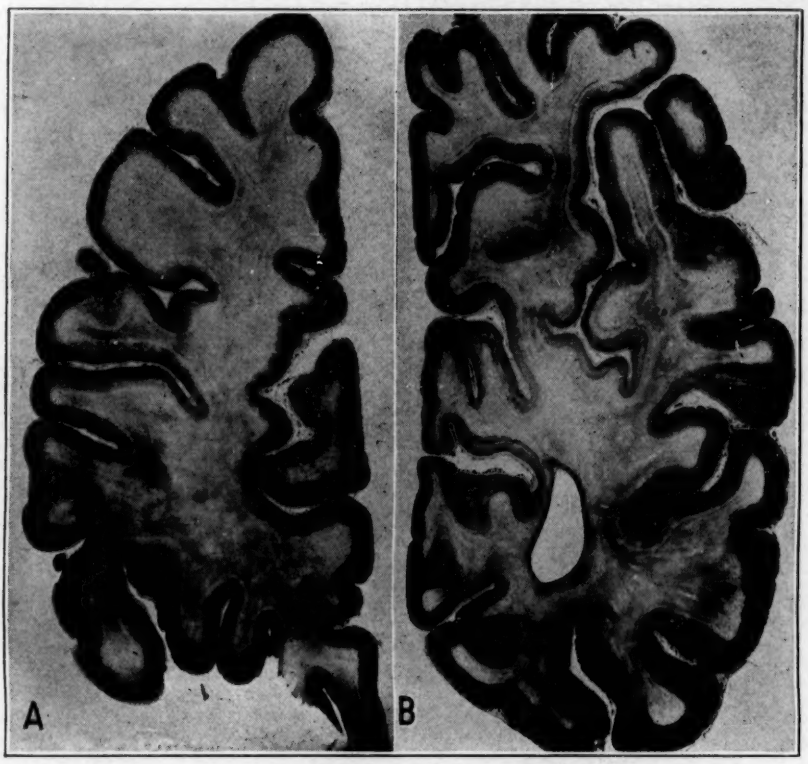

Fig. 3.—Coronal sections of the frontal (*A*) and the occipital (*B*) lobe in the Weigert preparation, showing absence of myelinated fibers. (The lipoids of the cortex are stained black.)

features of gemästete glia; others had long and numerous dendritic processes. Dense fibrillary gliosis was nowhere demonstrable with Holzer's method, but in the whole white matter a delicate meshwork of glia fibers could be detected.

In Hortega's preparation the microglia showed considerable proliferation with frequent transformation in compound granular corpuscles. While the fat-laden cells which were scattered in the demyelinated areas were filled with granules that stained palely with the scarlet red and sudan III, the gitter cells collected about the blood vessels stained bright red with scarlet red. This contrast in the staining property was striking in the Alzheimer VI preparation; the fatty granules

of the neurons and of the macroglia cells stained dark red whereas the perivascular compound granular corpuscles were black.

Blood Vessels: Perivascular infiltrations were often striking in the white matter (fig. 5); they were made up only of gitter cells, no hematogenous elements being seen. The walls of the vessels were otherwise normal. No mulberry-like cells were observed.

Cerebellum: Decided shrinkage of the folia was visible. The molecular layer contained a larger number of swollen glia cells, the cytoplasm of which was filled with lipoids. Small masses of lipoids were also found in places that apparently corresponded to branchings of dendrites of Purkinje's cells. The last had practically disappeared, and the Bergmann glia cells had proliferated to a marked degree (fig. 6). The few remaining Purkinje cells showed bizarre shapes, and

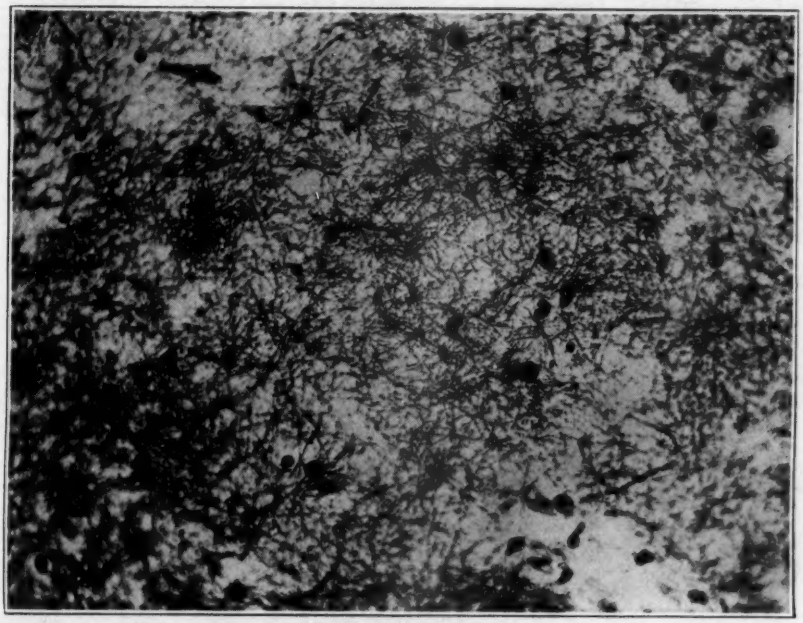

Fig. 4.—Glia proliferation in the white matter (Holzer stain; medium power).

the dendritic processes exhibited bulbous swellings of varying forms. The Bielschowsky method showed that the basket fibers together with the mossy and clumping fibers were reduced in number. Nodular swellings, apparently connected with the axons of the Purkinje cells, were rarely observed. The granular layer appeared thinner than normal and the granular cells decidedly reduced in number.

The cells of cerebellar nuclei showed the characteristic picture of swelling and infiltration of lipoids. Numerous cells had dropped out, and there was considerable increase of glia fibers in Holzer preparations. In the white matter of the cerebellum there was the same destruction of myelin which was observed in the brain.

Pia: Cellular infiltration (fig. 7) appeared, which consisted mainly of round cells loaded with fatty substances.

Viscera: The viscera showed no changes of special significance. Particular attention was paid to liver and spleen; in a large number of sections stained with hematoxylin and eosin, scarlet red, sudan and ferric hematoxylin, no changes suggesting Niemann-Pick disease were observed. The endocrine glands were not examined histologically.

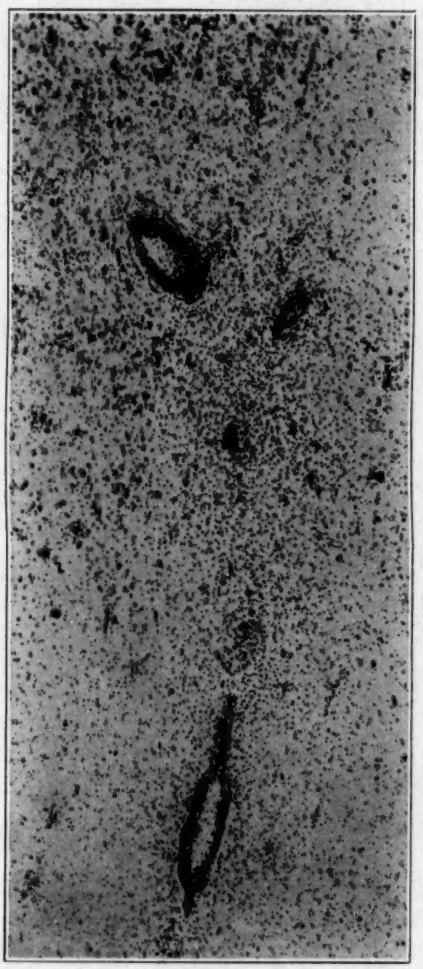

Fig. 5.—Perivascular infiltrations in the white matter (Nissl stain; low power).

Chemical Investigation.—In the attempt to isolate the lipoid stored in the nerve cells, extractions were made according to the method of Klenk.[2] Small pieces (420 Gm.) of fresh cortex of the brain which had been preserved in acetone in

2. Klenk, E.: Ueber die Natur der Phosphatide und andere Lipoide des Gehirns und der Leber bei der Niemann-Pickschen Krankheit, Ztschr. f. physiol. Chem. **235**:24, 1935.

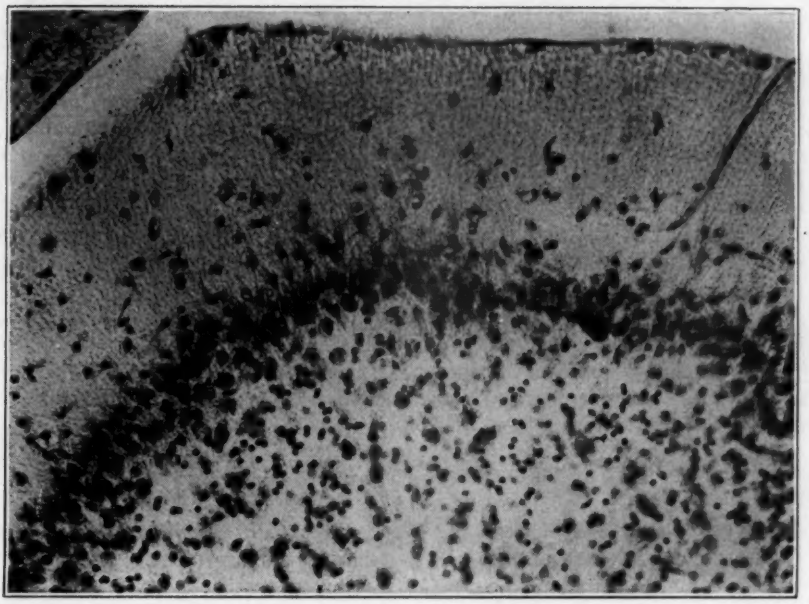

Fig. 6.—The cerebellum in the Nissl preparation, showing disappearing of the Purkinje cells and the proliferation of Bergmann glia.

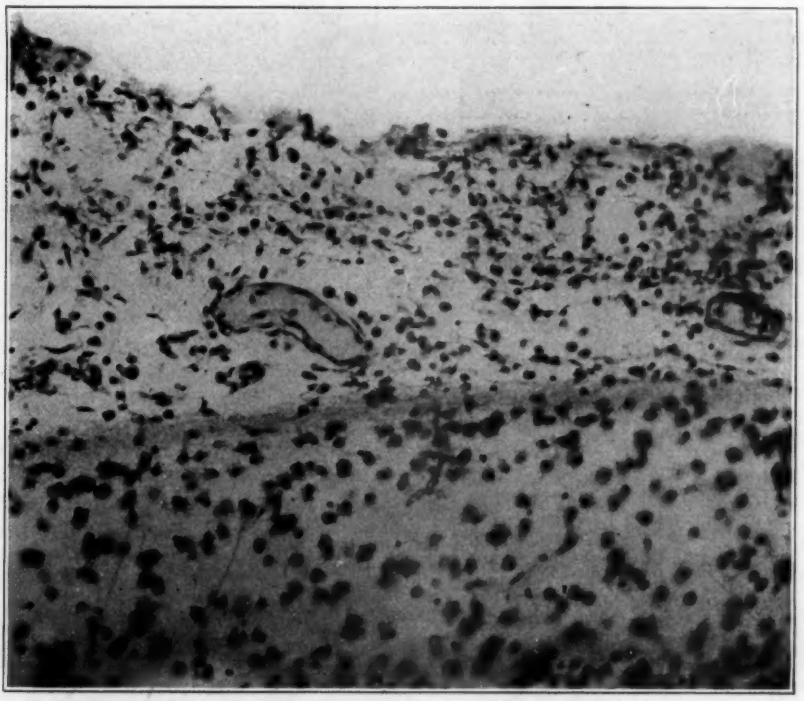

Fig. 7.—Infiltration of the meninges with fat-laden cells (Nissl stain; medium power).

an atmosphere of carbon dioxide were successively extracted in a Soxhlet apparatus with acetone and ether. A fraction of lipoid insoluble in cold acetone and cold ether was thus partially extracted but separated out immediately from acetone, and after standing overnight at a temperature of 0 C (32 F.), separated from ether. This fraction was suspended in ether, centrifugated and dried in vacuum; it weighed 1.68 Gm. The combined ether was strongly reduced and the etherosoluble phosphatides (lecithin and cephalin) were precipitated with acetone. A small amount of glycerophosphatides remained in the acetone extract. This was therefore evaporated, the residuum dissolved in ether, the ether strongly reduced and the etherosoluble phosphatides precipitated again with acetone. The total lecithin and cephalin dried in vacuum over phosphorus pentoxide weighed 4.23 Gm.

The remaining combined acetone was evaporated. The residuum, which contained mainly cholesterol and neutral fat, weighed approximately 5 Gm. No attempt was made to purify this fraction.

The brain substance, then, was extracted with a mixture of methyl alcohol and chloroform (3:1). The main fraction of ethero-insoluble and acetone-insoluble lipoids thus extracted was precipitated with acetone from the reduced mixture. This protagon fraction weighed 6.95 Gm. The results of the extractions are presented in the table.

Extractions From the Brain of a Child with Amaurotic Family Idiocy of the Late Infantile Type

Extraction	Dry Matter 40.8 Cholesterol	Glycero-phosphatides	Protagon
Acetone	4.6	1.01	1.11
Ether	1.4	3.22	0.57
Methyl alcohol and chloroform	...	....	6.95
Total	5.2	4.2	8.73
Dry matter, %	13	10	21

The protagon fraction, which contains sphingomyelin and cerebrosides, showed a ratio of nitrogen to phosphorus of 1:1.3. In order to obtain pure sphingomyelin, the crude product was dissolved in 10 units of methyl alcohol, impurities were precipitated off with cadmium acetate, the excess of acetate was removed with hydrogen sulfide, and the product obtained after evaporation of the methanol was recrystallized from ethyl acetate and pyridine. About 2 Gm. of a white powder was thus obtained which showed a strong positive Molisch reaction and a ratio of nitrogen to phosphorus of 1:1.3. Further purification was attempted by precipitating the cerebrosides from the solution of the lipoids in a mixture of benzene alcohol (5:1), with ethyl alcohol, following the direction of Levene.[3] This procedure was repeated twice. The pure sphingomyelin thus obtained melted at a temperature between 200 and 210 C. when recrystallized from ethyl acetate. The yield was less than 0.2 Gm. From the pyridine solution and from the precipitate in the benzene alcohol, a lipoid was isolated containing galactose and phosphorus. This lipoid was not examined further.

COMMENT

The clinical features of the case here recorded, excepting the abnormal size of the head, are those of the late infantile type of amaurotic idiocy. The absence of macular alterations, the age at which

3. Levene, P. A.: On Sphingomyelin, J. Biol. Chem. **24**:69, 1916

death intervened, and the occurrence of a neurologic syndrome closely resembling decerebration fit well into the clinical picture described by Bielschowsky,[4] Hassin,[5] Marinesco,[6] Greenfield and Nevin,[7] Schlesinger [8] and others. The remarkable clinical feature of this case was the presence of megalocephaly. Although this symptom was observed in a few cases of the literature (Savini-Castano,[9] Bielschowsky,[4] Steegmann and Karnosh [10]), in the majority of late infantile and in juvenile cases shrinkage of the brain rather than enlargement is encountered. Only in Steegmann's [10] case did the brain exceed in weight the one recorded here.

The pathologic changes of the neuron cells corresponded to those which numerous investigators have previously described as characteristic of the infantile type of amaurotic idiocy. It will be noted that, as often recorded concerning the late infantile type, the cells in which swelling occurred rarely acquired those bizarre forms characteristic of the infantile type and swelling of dendrites was almost entirely lacking. The decided cerebellar atrophy is another pathologic feature characteristic of, although not limited to, the late infantile type. Bielschowsky's [4] contention that centripetal formations are well preserved in this type of lesion, the cerebellar atrophy being electively centrifugal in character, appears inconsistent with the findings in the present case, in which the outstanding feature was a disappearance of the Purkinje cells with proliferation of Bergmann's glia.

The severe and diffuse demyelination which was found in the present case is worthy of a brief comment. The hypothesis that an arrest of myelin development had occurred fails to explain the pathologic features, which indicated that an active process of myelin destruction was taking place. On the other hand, that the demyelination was secondary to

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4. Bielschowsky, M.: Ueber spätinfantile familiäre amaurotische Idiotie mit Kleinhirnsymptomen, Deutsche Ztschr. f. Nervenh. **50**:7, 1914.

5. Hassin, G. B.: Amaurotic Family Idiocy: Late Infantile Type (Bielschowsky), with Clinical Picture of Decerebrate Rigidity, Arch. Neurol. & Psychiat. **16**:708 (Dec.) 1926.

6. Marinesco, G.: Nouvelles contributions à l'étude de la forme tardive de l'idiotie amaurotique (type Bielschowsky) et à son mécanisme biochimique, J. f. Psychol. u. Neurol. **431**:1, 1930.

7. Greenfield, J. G., and Nevin, S.: Amaurotic Family Idiocy: Study of a Late Infantile Case, Tr. Ophth. Soc. U. Kingdom **53**:170, 1933.

8. Schlesinger, B.; Greenfield, J. A., and Stern, R. O.: A Case of Late Infantile Amaurotic Idiocy with Pathological Report, Arch. Dis. Childhood **9**:1, 1934.

9. Savini-Castano, T., and Savini, E.: Beitrag zur Aetiologie, Pathogenese und pathologischen Anatomie der Tay-Sachsschen familiären amaurotischen Idiotie, Ztschr. f. Kinderh. **7**:321, 1913.

10. Steegmann, A. T., and Karnosh, L. J.: Infantile Amaurotic Family Idiocy, Am. J. Psychiat. **92**:1913, 1938.

lesions of the nerve cells, as contended by Santha [11] in discussing a case of infantile amaurotic idiocy with areas of demyelination, seems improbable in the present case, since the disproportion between the well preserved cortical cytoarchitecture and the severe demyelinating process was marked.

The lesion of the white matter bears striking similarity to the infantile group of familiar diffuse sclerosis ("leukodystrophy" of Bielschowsky [12]). The two main pathologic features of this condition, viz., the involvement of the whole white matter and the presence in the glia cells of so-called prelipoids, were evident in the present case. It appears therefore that two morbid processes, amaurotic idiocy and leukodystrophy, were present in the same patient. It will be noted that other cases of amaurotic idiocy reported in the literature (Bielschowsky,[4] Ostertag,[13] Globus,[14] Richter and Parmelee,[15] Steegmann and Karnosh [10]) showed diffuse demyelination similar to that found in the present case. Moreover, in a typical case of leukodystrophy described by Wicke [16] swellings of neurons, similar to those occurring in amaurotic idiocy, were found in some regions of the cerebral cortex. This frequent association of two different degenerative diseases of the central nervous system in the same person appears to indicate that similar pathogenic mechanisms might be operating in the two conditions.

The nature of the pathologic process which is at the basis of amaurotic idiocy is still the object of much discussion. The problem has received new impulse since Bielschowsky [17] and Spielmeyer [18] stressed the occurrence of visceral lesions characteristic of Niemann-Pick disease in cases of amaurotic idiocy and expressed the view that both conditions may be different localizations of the same altered lipoid

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11. Santha, K.: Ueber drei reine, von Niemann-Pickscher Krankheit verschonte Fälle der infantil-amaurotischen Idiotie, Arch. f. Psychiat. **93**:675, 1931.

12. Bielschowsky, M.: Ueber familiäre diffuse Sklerose, J. f. Psychol. u. Neurol. **36**:131, 1928.

13. Ostertag, B.: Entwickelungstörungen des Gehirns und zur Histologie und Pathogenese besonders der degenerativen Markerkrankung bei amaurotischer Idiotie, Arch. f. Psychiat. **75**:355, 1925.

14. Globus, J.: Ein Beitrag zur Histopathologie der amaurotischen Idiotie, Ztschr. f. d. ges. Neurol. u. Psychiat. **85**:424, 1923.

15. Richter, R., and Parmelee, A. H.: Late Infantile Amaurotic Idiocy with Marked Cerebral Atrophy: Clinical and Anatomic Report of Case, Am. J. Dis. Child. **50**:111 (July) 1935.

16. Wicke, R.: Ein Beitrag zur Frage der familiären diffusen Sklerosen und ihrer Beziehung zur amaurotischen Idiotie, Ztschr. f. d. ges. Neurol. u. Psychiat. **162**:741, 1938.

17. Bielschowsky, M.: Amaurotische Idiotie und lipoidzellige Splenohepatomegalie, J. f. Psychol. u. Neurol. **36**:103, 1938.

18. Spielmeyer, W.: Störungen des Lipoidstoffwechsels bei Erbkrankheiten des Nervensystems, Klin. Wchnschr. **12**:1273, 1933.

metabolism. This opinion, however, has found no general acceptance. In the attempt to clarify this debated question, it may be of assistance to divide the cases of amaurotic idiocy and Niemann-Pick disease into three groups: (*a*) cases of amaurotic idiocy without visceral lesions of the Niemann-Pick type; (*b*) cases in which amaurotic idiocy is associated with Niemann-Pick disease; (*c*) cases of Niemann-Pick disease without brain lesions of the Tay-Sachs type. The problem is whether all these conditions are manifestations of the same pathologic process, which is generalized (group *b*) or localized either to the brain (group *a*) or to the spleen and liver (group *c*).

Histologic criteria of differentiation between the brain lesions of groups a and b have been brought forward by Schaffer [19] and Santha.[11] These authors, who claimed that Tay-Sachs disease is a primary degeneration of the hyaloplasm affecting electively neuroectodermic structures, maintained that meningeal and perivascular infiltration with lipoid cells is absent in pure cases of amaurotic idiocy. Moreover, the transport of fat is carried on by glia elements in the cases of group *a*, by histiocytes in those of group *b*. In the present case, which undoubtedly belongs to group *a*, meninges and perivascular spaces were infiltrated with lipoid cells; microglia and adventitial elements were loaded with fatty-like substances. However, the mesodermic reaction might be referred to the demyelinating process which complicated the pathologic picture.

Since a common characteristic of the three groups of cases is an abnormal cellular storage of lipoids, it appears that biochemical investigations directed to the identification of the lipoids involved in each of the three groups are most likely to be fruitful. In cases of Niemann-Pick disease (group *c*) evidence has been produced that the lipoids which infiltrate liver and spleen are phosphatides, especially sphingomyelin (Klenk,[20] Tropp and Eckardt [21]). In 1 case of association of Niemann-Pick and Tay-Sachs disease (group *b*) Klenk [2] reported that the content of sphingomyelin of the brain was considerably above normal. There is, therefore, evidence that in these two groups the same lipoid is stored in the brain, spleen and liver. As far as pure cases of Tay-Sachs disease (group *a*) are concerned, the results of the extractions herein reported indicate that a decided increase of protagon occurs. It will be noted that the determinations were made on the cerebral cortex only, excluding the white matter. This was done for two reasons: First, histologically the lipoids were found to be stored mainly

19. Schaffer, K.: Grundsätzliche Bemerkungen zur Pathogenese der amaurotischen Idiotie, Monatschr. f. Psychiat. **84**:117, 1932.

20. Klenk, E.: Ueber die Natur der Phosphatide der Milz bei der Niemann-Pickschen Krankheit, Ztschr. f. physiol. Chem. **229**:151, 1934.

21. Tropp, C., and Eckardt, B.: Sphingomyelin bei Niemann-Pickscher Krankheit, Ztschr. f. physiol. Chem. **243**:38, 1936.

in the cells of the cortex, and second, the myelin sheaths of the white matter, which normally contain a large amount of protagon, were destroyed. A hypothetic increase of protagon in the nerve cells would obviously have been masked by the actual decrease of protagon in the white matter had both gray and white matter been used for the extraction.

Although exact figures concerning the protagon content of the cerebral gray matter are not available in the literature, control extractions showed it to be about 3 per cent of the dry matter in the normal brain. The protagon was therefore increased 6 to 7 times in the present case. In this respect the disease is strictly related chemically to the two conditions showing cellular infiltration with protagon, i. e., Gaucher's disease and Niemann-Pick disease, the former characterized by storage of kerasin, the latter by that of sphingomyelin. However, the exact chemical nature of the lipoid of the protagon fraction infiltrating the neurons in Tay-Sachs disease remains undetermined. That sphingomyelin is not chiefly responsible for the increase of lipoid is evidenced by the low ratio of nitrogen to phosphorus in the protagon fraction and by the very small final yield of pure sphingomyelin. In conclusion, as far as chemical evidence goes, amaurotic idiocy appears to be a different condition from Niemann-Pick disease, as already noted by Epstein [22] and more recently by Klenk.[23] This observation will explain the absence of splenic and hepatic lesions of the Niemann-Pick type in the present case as well as in the other cases of group *a*.

The fact of the frequent occurrence of cases of group *b* remains to be explained. That the combination of Niemann-Pick and Tay-Sachs diseases in the same person is merely accidental can obviously be excluded, both conditions being very rare. It has been observed that in Gaucher's disease lesions of the nervous system do occur, being characterized by swelling of the neurons which are loaded with lipoids (Lindau [24]). It can reasonably be assumed that in Niemann-Pick disease similar involvement of the nervous system is frequently observed, resulting in swelling of the neurons and in infiltration with sphingomyelin. In this last instance the clinical picture and the pathologic lesions are strikingly similar to those of Tay-Sachs disease, as should

22. Epstein, E.: Ueber das gegensatzliche Verhalten der lipoidchemischen Beschaffenheit des Gehirnes bei Niemann-Pickscher Krankheit und infantiler amaurotischer Idiotie vom Typus Tay-Sachs, Virchows Arch. f. path. Anat. **293**: 135, 1934.

23. Klenk, E.: Die Fettstoffe des Gehirns bei amaurotischer Idiotie und Niemann-Pickscher Krankheit, Ber. ü. d. ges. Physiol. u. exper. Pharmakol. **96**: 659, 1936.

24. Lindau, A.: Case of Gaucher's Disease, Acta path. et microbiol. Skandinav. **5**:22, 1928.

be reasonably expected in conditions so similar in nature, but the chemical characteristics of the lipoid involved in the disordered metabolism are different.

SUMMARY

A study is presented of a case of late infantile amaurotic idiocy with megalocephaly. Pathologically, typical lesions of amaurotic idiocy associated with extensive demyelination were found. Chemically, there was a marked increase of lipoids of the protagon fraction but no significant increase of sphingomyelin. The relationship of Niemann-Pick disease to amaurotic idiocy is discussed; it is concluded that the latter is not identical with the former, although strikingly similar to it in symptoms, pathologic aspects and chemical constitution.

Miss Hannah R. Folsom gave valuable technical assistance.

PULMONIC INTERSTITIAL AND MEDIASTINAL EMPHYSEMA

REPORT OF A FATAL CASE IN WHICH THE EMPHYSEMA OCCURRED IN A CHILD AS A RESULT OF THE ASPIRATION OF PEANUT FRAGMENTS

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AND
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Although interstitial emphysema of the lungs and mediastinum has been known for a long time, there has recently been a revival of interest in it. Many of the papers on that condition, however, have dealt with its occurrence among adults and with instances in which it promptly cleared up. We here describe the condition as it occurred in a young child in whom it rapidly progressed to a fatal ending and in whom the initial cause was the impaction of peanut fragments in the right main bronchus.

REPORT OF CASE

J. B., a white girl of 22 months, previously healthy, was admitted to the Children's Hospital on Nov. 23, 1937. Three days before, on November 20, while chewing a mouthful of peanuts, she took a sudden deep breath and aspirated a number of the fragments. She immediately choked, coughed and became blue. She continued to have coughing spells and on November 22 was described as feverish. On that day a few pieces of peanut were removed through a bronchoscope.

When she was examined on admission to the Children's Hospital, where she remained until her death, the sounds on the right side of the chest were much decreased, and percussion revealed increased dulness over the base of the right lung posteriorly. At 3 p. m. the temperature was 100.3 F., the pulse rate 150 and the respiratory rate 60. The color was good. The urine showed traces of albumin and sugar. A roentgenogram of the chest showed atelectasis of the lower lobe of the right lung; it was from the bronchus supplying this lobe that the pieces of peanut had been removed the day before. The mediastinum was shifted to the right. Thus there was dislocation of the heart and of both hili. There was obviously an overinflation of the left lung but no trace of pneumothorax.

At 7 p. m. on the same day the child was put in an oxygen tent. There was marked diaphragmatic breathing. Later that night she became restless and terrified and was using the accessory respiratory muscles. No cyanosis was noted. To relieve the respiratory distress a tracheotomy was performed at 8: 30 p. m.

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On November 24 no improvement was noted. At 4 p. m. the respirations were labored. Cyanosis was then not evident. The temperature was 103.6 F., the pulse rate 145 and the respiratory rate 64. Fine moist rales were heard in the right

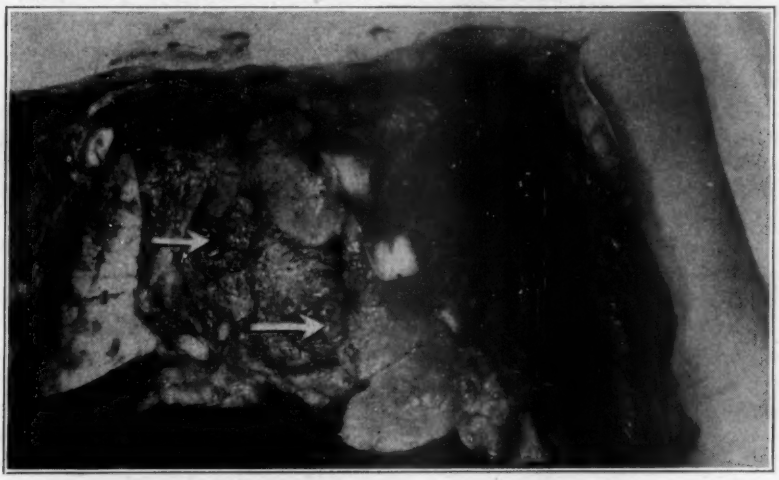

Fig. 1.—The freshly opened thorax, showing air blebs (indicated by the white arrows) in the loose tissue over the parietal pericardium as well as the contracted right lung and the anterior parts of the overexpanded left lung.

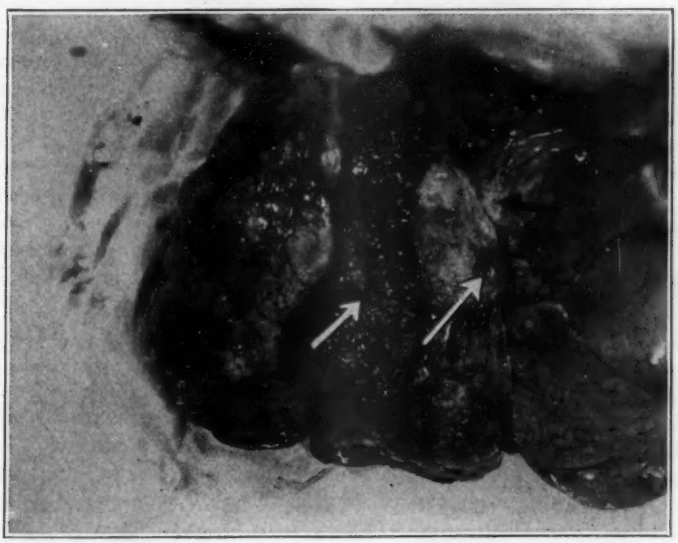

Fig. 2.—The fresh lungs and mediastinum from the front, after their removal from the thorax. Air blebs (white arrows) are seen over the pericardium; the subpleural air vesicles at the root of the left lung are also shown (black arrow).

lung posteriorly. At 11 p. m., she was restless, refusing fluids; slight cyanosis was seen. The temperature was 103 F., the pulse rate 160, and the respiration rate 60.

On November 25, the fifth day of the illness, at 7 a. m. the temperature was 103 F., the pulse rate 170 and the rate of respiration 62. There was decided prostration, and the lips and face were cyanosed. Fine moist rales were again heard in the lower third of the right lung, and there was evidence of consolidation. In the lower half of the left lung fine rales were heard. The child was evidently dying, suffering chiefly from failing circulatory and respiratory systems. She died at 1:35 p. m., after an illness of less than five days' duration.

Autopsy.—The postmortem examination was performed at the medical school of the University of Western Ontario two hours after death. The body was well nourished and 38 inches (96.52 cm.) long. No subcutaneous emphysema was noted in the cervical tissues.

Contents of the Thorax: When the pleural compartments were opened, no gas was heard issuing from either side. Tests revealed no pneumothorax. Both pleural sacs were free from adhesions, exudate and excess fluid. Removal of the sternum and anterior parts of the ribs disclosed in the cellular tissue of the mediastinum numerous air bubbles, varying in size. The right lung was collapsed, and the lower lobe was small. The left lung, much larger than the right, was pale and distended with air. The most striking feature revealed by gross examination was well marked mediastinal and radicular subpleural emphysema. Gas bubbles were easily seen under the pleura at the hilus of each lung, in the anterior and the superior mediastinum, over the anterior surface of the thymus, in the interstitial tissue overlying the parietal pericardium and extending along the course of the great vessels into the root of the neck. Except for this emphysema at the root of the neck there was at the time of autopsy no emphysema of the cervical region. However, when the tracheotomy was being done the operator noted that a bloody froth issued from the wound, although the trachea was intact.

Photographs of the fresh lungs, heart and adnexa were taken at the time of autopsy. In figures 1, 2 and 3 large blebs of air are seen in the loose tissue overlying the parietal pericardium. The bubbles of air under the pleura of the root of the left lung are shown in figure 2, and under that of the right lung in figure 3, the lung in each instance being retracted. In these figures the small right lung contrasts sharply with the large left one. The latter has, at the time the photograph was made, apparently lost but little in size after the thorax was opened.

The contents of the thorax were then removed en masse. No air was noted in the peritoneal cavity or retroperitoneal region. The other organs appeared normal.

Lungs, Heart and Mediastinum Examined en Masse.—The mass of organs consisting of lungs and trachea in normal undisturbed relation to the heart and surrounding tissues was dealt with as follows: A cannula was tied into the trachea, and Bouin's fluid was run into the bronchial tree at low pressure. The fluid entered the left lung more readily than the right. There was no leakage of fluid from any part of either lung, including the root. When distention of the left lung had reached approximately the normal limit of inspiration, the tubing was clamped and the entire mass was immersed in Bouin's fluid and allowed to remain there until thoroughly hardened. The right lung was, as it had been before, considerably smaller than the left. The lower lobe of the right lung was much shrunken and obviously atelectatic.

Photographs were taken from the front (fig. 4) and back (fig. 5) with the lungs in this detached and fixed condition. In these photographs the air blebs do not stand out as clearly as in the pictures taken with the lungs in the fresh condition. Much of the air has been replaced by fixing fluid. The atelectatic lower lobe of the right lung is clearly displayed in figure 5.

Roentgenograms of the material in this condition were rather dense, as the lungs were full of fluid; they showed nothing of interest.

Roentgen Study of the Bronchial Tree After Injection of Iodized Poppyseed Oil: As much of the fluid as possible was drained from the bronchial tree, and iodized poppyseed oil was injected into it; a roentgenogram was then taken of the two lungs. There was much more oil (as indicated by the shadows) in the left lung than in the right. In the left lung, in spite of the fixing fluid which remained in the peripheral lung tissue, some of the oil penetrated into that tissue, particularly of the upper region; in the right lung, on the other hand, it did not so diffuse but was limited almost altogether to the large bronchi of the hilus, except in the upper region, which was air holding in light. In the basal part of the lung there was no oil at all. The shadows in the right stem bronchus and in the main bronchi were thin

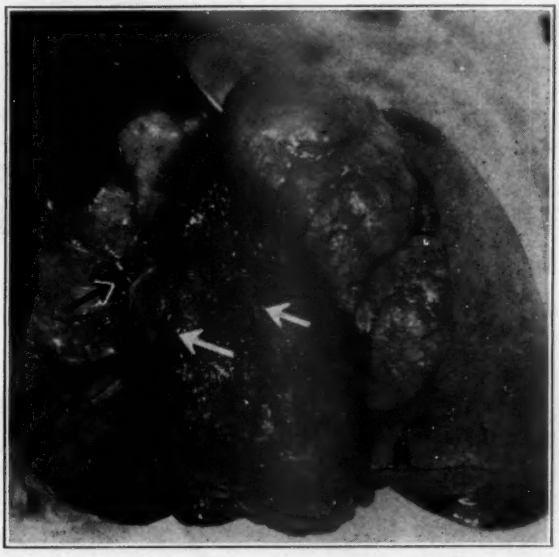

Fig. 3.—A portion of the same material as in figure 1, photographed to show the subpleural air vesicles at the root of the right lung (black arrow). The "puffy" appearance of the left lung is to be noted. Precordial air blebs are again shown (white arrows).

and broken, whereas in the left stem bronchus the shadow was almost solid. In brief, the results of this experiment showed that there was a block in the main stem of the right bronchial tree.

Detailed Examination of the Trachea, Lungs and Mediastinal Contents.—After having stood in Bouin's fluid for several days, the lungs were removed from the mediastinum by severance of the roots with a sharp knife. During the long immersion in the fixing fluid there was a loss of some of the air. At the time of removal from the fluid, the bubbles over the pericardium were mostly filled with fluid and were inconspicuous.

Trachea and Main Bronchi: An important observation was made in the right main bronchus just beyond the bifurcation. Several (at least six) pieces of hard, yellowish brown peanut were revealed here, surrounded by exudate. Most of them

Fig. 4.—The two lungs seen from the front, distended with fixative injected through a cannula in the trachea (shown). The inequality in size of the lungs is plain.

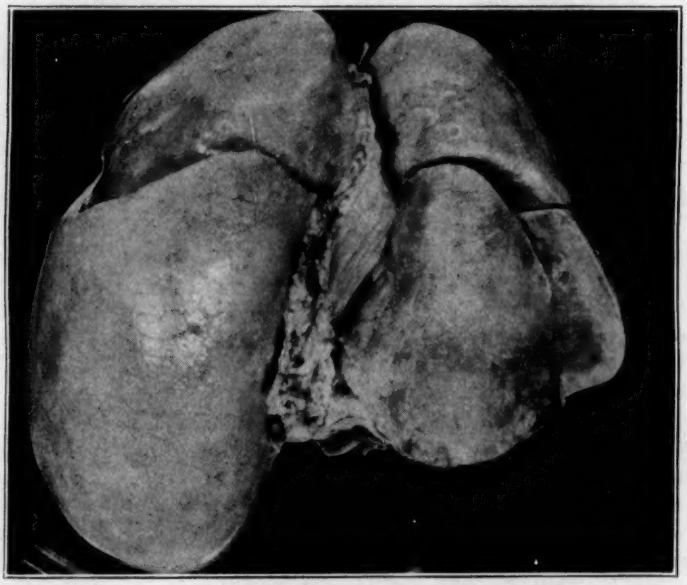

Fig. 5.—The two lungs seen from behind, after the fixation illustrated in figure 4. The atelectatic lower lobe of the right lung is clearly shown.

were small, broken pieces, about 2 mm. in diameter, but one piece was elongated, cylindric, 4 mm. in diameter and 1 cm. long. This mass was evidently the cause of the pathologic condition.

Right Lung: Gross observations of serial sections. Thick sections of the substance of the right lung were made in the sagittal plane and were examined carefully with the low and high powers of the binocular microscope. There was emphysema of the interstitial tissue of the root region. Evidence of this was seen in the subpleural blebs in that region and has been mentioned. This emphysematous air, which was mainly in the vascular sheaths, did not penetrate deeply into the lung but rather was limited to the hilus. Its origin, therefore, was probably in the mediastinum. Careful inspection of the serial sections revealed no air in the vascular sheaths of the lung proper. The bronchi and bronchioli, especially

Fig. 6.—The surface of a section through the lower lobe of the right lung. Medium-sized bronchi plugged with exudate are seen. The pulmonary tissue is atelectatic and should be compared with that of the left lung shown in figures 9, 10, 11 and 12. The method of fixation was that described in the text (× 2.6).

the tissues near the hilus, were plugged with coagulated exudate. Figure 6 shows the exudate in the bronchi. There was an atelectatic condition in the inferior part of this lung, especially in the lower lobe. This can be appreciated from the section shown in figure 6, particularly when that section is compared with the sections from the left lung pictured in figures 9, 10, 11 and 12. No pneumonia was observed in the gross examination. The hilus glands seemed swollen, pale and soft. The upper and middle lobes were air containing, particularly above, where they tended to be emphysematous.

Microscopic Observations: In the right main bronchus the mucous membrane showed areas of necrosis and ulceration with fibrinopurulent exudate attached. The submucosa was congested and infiltrated with inflammatory cells.

In the hilus the bronchi were plugged with gross masses of mucopurulent exudate containing bacterial clumps. The bronchial mucosa showed necrotic ulcerated areas, and the bronchial walls were infiltrated. The peribronchial lymphatic vessels were dilated and prominent. In the peribronchial lymph glands the lymph sinuses were dilated and contained inflammatory cells which were also infiltrating the reticulum. Most of the pulmonary lung tissue in these sections was decidedly atelectatic. There was no actual pneumonia. The perivascular connective tissue contained large spaces (air bubbles), which had separated the pulmonary vessels from their surrounding connective tissue.

In the lower lobe the larger bronchi contained plugs of mucopurulent exudate. No pneumonia was observed. The alveoli were collapsed and markedly atelectatic.

The upper lobe posteriorly showed moderately overdistended pulmonary tissue; but the alveolar ectasia was not so marked as in the corresponding area in the left lung. This section contained no pneumonia but a few of the bronchioles enclosed masses of purulent exudate.

Summary of Detailed Examination of the Right Lung: The conclusions drawn from the clinical history, roentgenographic observations and initial examination of the thoracic contents in respect to the foreign bodies in the right bronchus and to the resultant atelectatic and inflammatory changes, were supported by the detailed examination of the right lung.

Left Lung: Gross Observation of Serial Sections. The section taken through the root showed much air in the connective tissue; the spaces containing the air were continuous with the blebs of the mediastinum. The lung was voluminous and pale. The tissue appeared overinflated. The lung was carefully cut into thick, sagittal sections with a sharp, thin knife; this was easily accomplished, as the material was firm and resistant.

The interior, particularly the hilus region, presented an amazing picture, in that the interstitial tissue was invaded by a large amount of air. Owing to the method used in fixation, the position of this air was preserved, and all its original relations could be ascertained. Much air was found in the vascular sheaths, dissecting and splitting the connecting tissue into delicate, cobweb-like strands. This was most conspicuous around the larger vessels, producing decided compression and collapse of these vessels from the pressure of the surrounding air. Figures 7 and 8 show this interstitial emphysema under low power. Collapsed pulmonic blood vessels were seen, often completely surrounded by air. Extending from the air-dilated vascular sheaths, there sometimes appeared in the connective tissue clefts which occasionally reached the bronchi. An interesting one was observed that split a trabecula of connective tissue as far as the pleura, under which it appeared as an elongated bleb (fig. 7). This detail of the air dissection is shown in higher magnification in figure 9. On the right side of the photomicrograph is seen a collapsed blood vessel completely surrounded by a great bleb of air. Toward the left it can be seen that the air cleaved widely the aforementioned trabecula of connective tissue, lying in which a collapsed ramus of the larger blood vessel is visible. Where the air reached the pleura it separated the masses of subjacent lung widely. The bleb so formed did not rupture; if it had done so a pneumothorax would have resulted.

Another detail from figure 7 is magnified in figure 10. To the right is seen a typical large air burrow, in which the collapsed blood vessel looks insignificant. To the right a large air bleb is seen to have elevated the pleura in the depths of the interlobar fissure. Between these two features is a smaller accumulation of air around a blood vessel. On examining the serial sections carefully with the naked eye and more minutely with the binocular microscope, it was seen

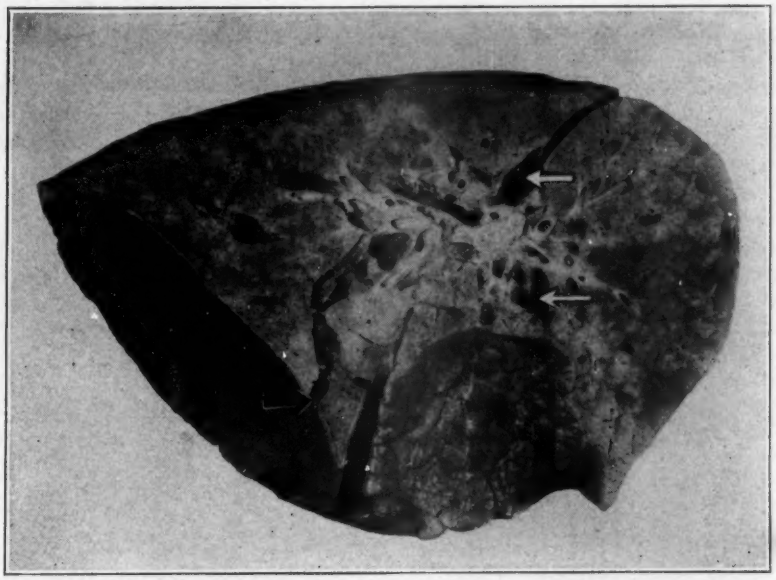

Fig. 7.—A sagittal section made through the left lung after fixation in the distended condition. The dissection by air of the vascular sheaths and related parts of the interstitial tissue is shown. An extension to the pleura, terminating in a subpleural bleb, is seen in the lower left portion of the photograph (black arrow). (This detail is shown in higher magnification in figure 9.) To the right of the center of this illustration is visible a subpleural bleb in the interlobular fissue (upper white arrow), and below it is a large ballooning of a vascular sheath (lower white arrow) (× 0.65). (Both of these features are shown in higher magnification in figure 10.)

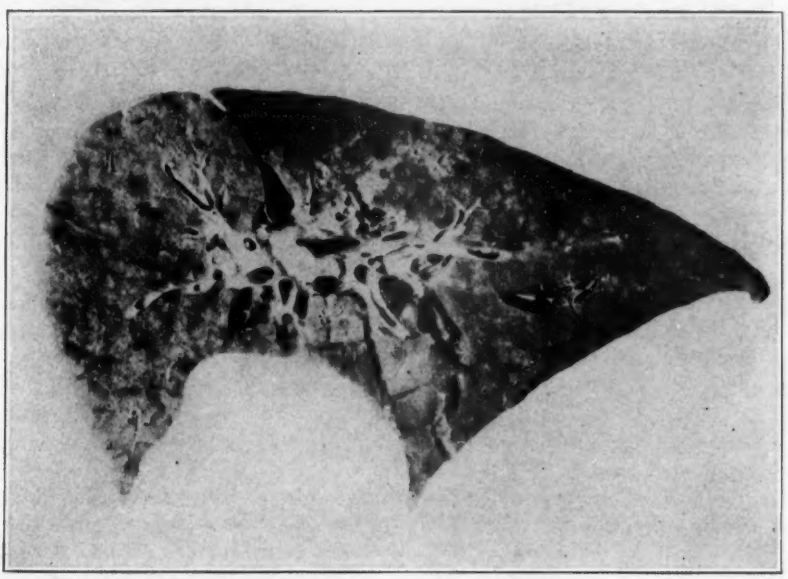

Fig. 8.—Another section from the left lung, showing further details of the interstitial emphysema. Toward the right tip a large, isolated, air-distended vascular sheath is seen (× 0.65).

that the inflation of the vascular sheaths involved small blood vessels, such as the one seen in figure 11, or still smaller ones, as that of figure 12. In these, as in the larger trunks, the lumen was narrowed or even obliterated by the air pressure.

The perivascular emphysema was more pronounced in the lower lobe, but occurred to some extent in the part of the upper lobe nearest the hilus. Patchy, firm, gray, consolidated areas were observed in the posterior aspect of the lower lobe 4 cm. from the apex and running from the pleural surface toward the hilus. The rest of the pulmonary tissue was hyperinflated.

The bronchi were carefully studied in these serial sections and found to be free from gross exudate; in this respect they were strikingly different from those of the right lung.

Microscopic Observations. The lumen of the left main bronchus, in contrast to that of the right bronchus, contained no exudate. Except for two small areas

Fig. 9.—An extension of an air dissection from a vascular sheath (at the right) through a strip of connective tissue to the pleura, which forms a bleblike covering. This covering has not ruptured. The cobweb-like nature of the connective tissue which has been infiltrated by the air is plainly shown. This illustration shows in higher power a detail of the section displayed in figure 7. The alveoli are ectatic (× 3⅓).

denuded of epithelium (an anomaly which might have been purely of mechanical origin), the mucous membrane was essentially normal, and cilia could be seen. The submucosa of this bronchus contained rather numerous polymorphonuclear leukocytes. A small lymph gland in the wall of the bronchus was normal.

The pulmonary tissue of the apex of the upper lobe showed alveolar ectasia. The bronchioles contained masses of purulent exudate, and mild pneumonia was present in small patches.

In the base of the upper lobe the picture was essentially similar, but there was slightly more extensive pneumonia.

The apex of the lower lobe posteriorly showed a well marked alveolar ectasia, with some purulent bronchitis and patches of pneumonia.

The condition of the midportion of the lower lobe posteriorly was much like that of the rest of the lung, but there was more extensive pneumonia. More pneumonic involvement appeared in this region than in all the other sections of the left lung.

Fig. 10.—A more highly magnified view of a part of the material seen in figure 7. On the left is a subpleural bleb, deep in the interlobar fissure. The covering pleura is intact. On the right is a huge air dissection, with a collapsed vessel, quite inconspicuous, in the center. Between these, a smaller, air inflated sheath is seen with a blood vessel near one side. The alveoli are ectatic (× 2¾).

Fig. 11.—A collapsed pulmonic blood vessel within a distended sheath; left lung, lower lobe. The overly distended surrounding lung tissue is visible (× 2¾).

Summary of Detailed Examination of the Left Lung: The outstanding anomaly in the left lung was the large amount of interstitial air, particularly in the distended sheaths of the pulmonary arteries and veins, but also in extensions from

these. The pulmonary blood vessels were so much compressed by this air that it is difficult in many instances to see how the blood could flow through them at all. It is obvious that the flow must have been much impeded. Correlated with this anomaly was the generalized alveolar ectasia. There was also some scattered bronchopneumonia, often mild.

Heart: The right auricle and ventricle were dilated and distended with clotted blood. This condition harmonized with the evident signs of circulatory obstruction in the left lung and in the mediastinum and was the only important feature shown by the heart, the valves being normal, the foramen ovale closed and the great vessels having a normal form and arrangement.

Other Organs: The thymus appeared normal, but there were large gas bubbles in the interlobular connective tissue. Venous congestion was observed in the kidneys. There was nothing to note in the liver, spleen or adrenal glands.

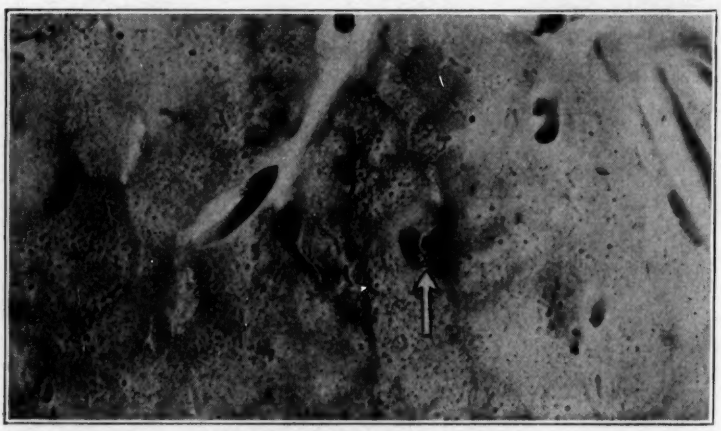

Fig. 12.—A small pulmonic blood vessel surrounded by a lesser quantity of air (white arrow) around it; left lung, near the apex (× 2 ⅔).

COMMENT

The child aspirated pieces of peanut into the right main bronchus, where they became impacted near the bifurcation. Not all of these pieces were removed by the bronchoscope, and the remaining fragments produced a brisk inflammation in the adjoining bronchial wall. Much exudate accumulated in this bronchus and its branches. This exudate, together with the fragments of peanut, plugged these bronchi and produced atelectasis of the right lung, particularly the lower lobe. There was evidence of this in the roentgenogram taken two days before death. Thus the volume of the right lung was greatly diminished, particularly in its lower part. Accordingly the left lung became voluminous in an effort to fill in the vacancy in the right pleural cavity, and this caused the mediastinum to be dislocated to the right. The effect of the extreme overinflation of the left lung was to put the alveoli under such a strain that doubtlessly

multiple ruptures occurred in them, allowing the air to leak into the sheaths of the finer pulmonary blood vessels. There was thus formed an interstitial emphysema, or, more specifically, a pulmonic perivascular emphysema. The air tracked back to the hilus along the perivascular sheaths in the manner described by one of us [1] and on into the mediastinum, from which it spread for some distance along the course of the great vessels into the neck. The observation made by the surgeon at the time of the tracheotomy, forty-one hours before death, is of great significance. After making the incision in the skin and dividing the muscles overlying the trachea, he observed bubbles of gas emerging. At first he thought he had nicked the trachea, but on sponging the wound dry he found he had not. These gas bubbles were due to the extension of the mediastinal emphysema into the neck. Therefore the aberrant air in the mediastinum and lungs could not have originated from the tracheotomy wound. Pneumoperitoneum was not found, and there was no pneumothorax. Although a subpleural bleb was noted, continuous with the artificial air spaces in the vascular sheaths, this bleb was not ruptured, and there was no leakage of fluid or residual air while the lungs were being filled with fixative. There was no evidence that the air holding parts of the right lung, although showing some alveolar ectasia, had allowed air to leak into the interstitial tissue of that side. It is certain, however, that there was some backing up of air into the right hilus from the mediastinum, and this process originated from the left lung.

We feel convinced, then, that the interstitial emphysema in the left lung and in the hilus region of each lung, together with the mediastinal emphysema, caused decided compression of, and obstruction to, the pulmonary and mediastinal circulation; this produced severe dyspnea, anoxemia and cyanosis as well as impeded action of the heart. The right side of the heart, it will be recalled, was observed at autopsy to be much dilated and filled with clotted blood. The pathologic picture in the thorax of this child was closely similar to that described by one of us [1] after experiments on overinflation of lung tissue in living cats into whose lower lobe of the right lung a blast of air was blown. The leak holes arising in the stretched and weakened floors of those alveoli which overlie the smaller pulmonic blood vessels were numerous and small. Their position has so far been indicated only by the use of the gelatin-carmine method.[2]

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1. Macklin, C. C.: Pneumothorax with Massive Collapse from Experimental Local Over-Inflation of the Lung Substance, Canad. M. A. J. **36**:414-420 (April) 1937.

2. Macklin, C. C.: The Site of Air Leakage from the Lung Alveoli into the Interstitial Tissue During Local Over-Inflation in the Cat, Anat. Anz. (supp.) **85**:78-81, 1938.

In the lungs of this child the overinflation was compensatory: The left lung particularly, and the upper part of the right lung to a lesser degree, expanded unduly to make up the space lost through diminution in volume of the right lung, especially the lower lobe of the right lung. The greatest amount of alveolar ectasia was in the lower part of the left lung, and this was at the same level as the region of greatest diminution of volume in the right lung. It has been pointed out that atelectasis, by diminishing lung volume, favors the leakage of air into the interstitial tissue because of the compensatory alveolar ectasia.[3] The weakening of the alveolar walls which the strain produces makes the alveoli incompetent to contain air; and since the line of least resistance for the air is into the vascular sheaths,[1] the sheaths become invaded by air. Coughing seems to facilitate leakage of air into the sheaths, and the shortening and lengthening of the pulmonic blood vessels, associated with similar movements in the bronchial tree during expiration and inspiration, respectively,[4] doubtless serve to move the train of bubbles along toward the hilus.

There is no doubt that these spaces formed by cleavage contained air in life. That they were not due to the technic of fixation, for instance, is indicated by their absence from lungs which were fixed in the same way but which had no interstitial emphysema. Then, too, when the freshly cut sections of the left lung were weighted down in Bouin's fluid so that it submerged them completely and were allowed to stand thus overnight, many large bubbles of air were observed in the morning overlying the clefts and perivascular tunnels, a condition which showed that the air which originally occupied these clefts and tunnels had risen to the surface and had been replaced by the fixing fluid. Finally, it is taken for granted that this gas is air, for it could hardly be any other gas. There was nothing to suggest the action of the gas bacillus, for instance; the autopsy was performed almost immediately after death.

The tracheotomy with intubation was done because it was thought that the respiratory distress was occasioned by an edema of the glottis following the bronchoscopy. That the dyspnea was not due to laryngeal obstruction, however, is proved by its persistence and even increase after the tracheotomy. Other possible causes having been absent, it must have been due to the presence of a large volume of air in the interstitial tissue of the lung and mediastinum.

In many cases of interstitial emphysema of the lungs and mediastinum the end result is favorable, as in the case of the athletic young man

3. Macklin, C. C.: Spontaneous Mediastinal Emphysema: A Review and Comment, M. Rec. **150**:5, 1939.

4. Macklin, C. C.: Air Transport Along the Sheaths of the Pulmonic Blood Vessels from Alveoli to Mediastinum and Some Clinical Implications, Arch. Int. Med., to be published.

described by Morey and Sosman [5] and in the series of 7 men reported by Hamman [6]; the air in such instances is speedily absorbed, and the patient returns to normal in a week or so, though he may have subsequent attacks. But in such cases as the one just described, in which reduction of the lung volume is great and, accordingly, the area of compensatory alveolar ectasia extensive, the interstitial emphysema is abundant and the obstruction to the circulation correspondingly serious. The prognosis seems to be less favorable among the young. In the lungs in this case, moreover, there was little escape for the mediastinal air, for the outlet into the tissues of the neck was slight, and there was no outlet into the retroperitoneum or into the pleural cavity. The circulatory embarrassment on account of the pressure of air in the mediastinum and lung was therefore great. This circulatory obstruction, together with the dislocation of the mediastinal contents and the added burdens resulting from the inflammatory conditions in the bronchi and lungs, brought about the termination of life in less than five days.

SUMMARY

A fatal case of pulmonic interstitial emphysema and mediastinal emphysema occurring in a child of 22 months and arising from aspirated pieces of peanut is described. Circulatory embarrassment from the pressure of this emphysematous air was the principal cause of death. This, we feel, is not a commonly recognized cause of death. The fact that the aberrant air distends the sheaths of the pulmonary blood vessels as it travels from the region of leakage from overdistended alveoli to the mediastinum is of great importance, for the vessels are thereby narrowed and even totally collapsed, so that the blood flow is accordingly impeded or actually stopped. The morphologic picture of the interstitially emphysematous lung, after special fixation, is presented, and the mechanics of invasion of air from the alveoli and of transfer of it along the vascular sheaths through the lungs is discussed.

Mr. Walter Downs prepared the photographs.

5. Morey, J. B., and Sosman, M. C.: Spontaneous Mediastinal Emphysema, Radiology **32**:19-22 (Jan.) 1939.

6. Hamman, L.: Spontaneous Mediastinal Emphysema, Bull. Johns Hopkins Hosp. **64**:1-21 (Jan.) 1939.

PROGRESSIVE FACIAL AND CROSSED HEMIATROPHY COMPLICATED BY TRANSIENT HYPOGLYCEMIA

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Progressive facial hemiatrophy is a rare disease, especially in childhood. Of extremely rare occurrence is crossed hemiatrophy.

ETIOLOGY

This disorder may occur at any period. It is, however, predominantly a disease of early life, beginning most commonly in the second decade. The two sexes are affected equally. The exact etiology is still obscure. Among the predisposing factors the following may be mentioned: (1) trauma, (2) acute infectious diseases, (3) toxic conditions, (4) dental diseases, (5) encephalitis and (6) tuberculosis. While a direct relation could not be demonstrated, these conditions have preceded the onset of facial hemiatrophy. It is interesting to mention that tuberculosis of the apexes of the lung has been found in addition to other pathologic conditions in most cases in which autopsy has been performed.

Often the disease may be associated with lesions in the region of the cervical sympathetic system. Paralysis of the brachial plexus is mentioned as a causative factor, and also diseases of the trigeminal nerve, though complete or partial section of the trigeminal nerve does not result in hemiatrophy. Cases of congenital involvement have also been reported.

The relation between this syndrome and scleroderma is not fully understood. Some authors contend that scleroderma is the etiologic factor, while others believe that facial hemiatrophy is merely a special form of scleroderma. It is noteworthy that there are a disappearance of fat and an atrophy of the skin in both conditions. Cassirer [1] and many

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1. Cassirer, R.: Die vasomotorisch-trophischen Neurosen, ed. 2, Berlin, S. Karger, 1912.

others have expressed the belief that facial hemiatrophy is only a variety of scleroderma, since it is often combined with sclerodermatic changes in other parts of the body.

Gliomatosis of the spinal cord and epilepsy have been observed in association with facial hemiatrophy, but their causal relation is not clear. Merritt, Faber and Bruch [2] mentioned the occurrence of cerebral calcifications in their 2 cases. They contended that the convulsive seizures were directly related to the calcified cerebral lesions, but they could not determine the relation of the intracranial process to the hemiatrophy.

Most observers attribute this condition to a disturbance of the sympathetic nervous system, and the accumulated evidence points strongly to a neurogenic origin. No endocrine disturbance can be considered as a primary cause of this disease, though the pituitary body, the thyroid and the pancreas have been cited as causative factors.

PATHOGENESIS

Numerous theories have been advanced to explain the mechanism involved in the pathogenesis of this syndrome. It becomes evident from the accumulated data that there is an involvement of the autonomic nervous system, though it is difficult to explain in what manner it is affected. Marinesco, Kriendler and Façon [3] stated the belief that the autonomic nervous system is implicated in maintaining the normal trophic function of the tissues. Dejerine and Mirale suggested that facial hemiatrophy is a result of the paralysis of the sympathetic fibers from the cervical portion of the spine. Others have claimed that the syndrome is produced not only by a lesion in the sympathetic chain but also by a disorder in the rami communicantes. Barrel [4] contended that a lesion of the inferior cervical ganglion was the cause of all the instances of facial hemiatrophy which came under his observation.

A pathologic condition of certain specific trophic centers in the midbrain has been advanced as a cause of this syndrome, though no one has ever demonstrated the existence of such centers. It is worth mentioning that evidence of organic lesions in the hypothalamus, the midbrain, the pons, the medulla and the upper parts of the cord has been observed not infrequently in patients suffering from hemiatrophy. Many patients also have presented Horner's syndrome. Neurologic pains, including hyperesthesia of the face, suggest in some cases an

2. Merritt, K. K.; Faber, H. K., and Bruch, H.: Progressive Facial Hemiatrophy: Report of Two Cases with Cerebral Calcification, J. Pediat. **3**:374, 1937.

3. Marinesco, G.; Kriendler, A., and Façon, E.: Sur la pathogénie de l'hémiatrophie faciale, Paris méd. **1**:269, 1932.

4. Barrel, E.: De l'hémiatrophie faciale dans ses rapports avec les lésions du ganglion cervical inférieur, Thesis, Lyon, no. 132, Lyon, Bourg, 1902.

involvement of the fifth cranial nerve. The sensory disturbance, however, does not follow the distribution of the trigeminal nerve. Cases have been reported in which this syndrome followed possible injuries to the cervical portion of the sympathetic trunk in the neck, such as those caused by operations for cervical adenitis, thyroidectomy, tumors of the neck and cervical ribs.

According to Archambault and Fromm,[5] this syndrome is due to a lesion of the sympathetic nervous system of a mixed variety, partly destructive and partly irritative, in which the destructive component probably predominates. It must be noted, however, that one does not find a disturbance of the autonomic nervous system in every case of facial hemiatrophy, especially in those in which the atrophy was spread beyond the region innervated by the sympathetic nervous system. Wartenberg[6] theorized that a chronic state of excitation in the autonomic nervous system, possibly due to a disorder of its central parts, plays a role.

It appears from the foregoing review that this syndrome may be produced in a variety of ways, but the exact nature of its pathogenesis is still just as obscure as its etiology. The evidence, though lacking in proof, points strongly to a disorder of the nervous system. We are of the opinion that facial hemiatrophy is due to a degenerative process of the central nervous system, including the autonomic.

PATHOLOGY

The atrophic changes are prominent in the skin, inducing a thinning of the skin, but the subcutaneous tissues also become involved. At times the atrophy of the subcutaneous tissues precedes that of the skin. The disease may also involve all the underlying tissues, the subcutaneous fat, the muscles, the cartilage and the bones. The tongue and the temporal and masseter muscles also may become involved. A thinning and discoloration of the hair may occur. Pigmentary anomalies have been commonly associated with facial hemiatrophy.

The atrophic process progresses, reaches its maximum intensity within five years and then becomes stationary.

In most cases in which autopsy has been performed, in addition to tuberculous lesions in the apexes of the lung an involvement of the inferior cervical ganglion has been noted, while in others there have been signs of neuritis in the peripheral portion of the trigeminal nerve with changes in the spinal nucleus of the same nerve. Interstitial

5. Archambault, L., and Fromm, N. K.: Progressive Facial Hemiatrophy: Report of Three Cases, Arch. Neurol. & Psychiat. **27**:529 (March) 1932.

6. Wartenberg, R.: Zur Klinik und Pathogenese der Hemiatrophia faciei progressiva, Arch. f. Psychiat. **74**:602, 1925.

neuritis of the gasserian ganglion and also gliomatosis were found in several cases. In Stief's [7] case lesions of the superior and inferior cervical ganglions and of the upper paravertebral ganglions were found on the side of the hemiatrophy. In the brain were noted vascular stasis, dilatation and necrosis.

HEREDITY

A neuropathic tendency is believed to be a predisposing factor by some observers. In the case we are about to report we were unable to obtain any history of such a tendency on either the maternal or the paternal side of the patient's family.

REPORT OF A CASE

History.—L. R. is a girl of Italian ancestry, the fourth child in the family. Her father and mother are living and well. There is no history of tuberculosis, epilepsy, vascular syphilis or mental disease on either side of the family. There are five other children, all of whom are normal in appearance and mentality.

The patient's birth and development were normal. She walked and talked at 9 months of age and cut her first tooth at 5 months. She had pertussis at 3 years. She was well, except for occasional colds, until the age of 5 years, when measles developed. Several months after the onset of measles her mother noticed a white spot about the size of a dime over the left scapular region. Two weeks later the mother observed that the child's face did not appear "just right" and that the hair in the left frontal region was becoming thin and white. No definite asymmetry could be noted at that time, although a deviation from normal was apparent.

One of us (G. P.) was then consulted, and on Nov. 29, 1926 the patient was sent to the Bellevue Hospital for observation and study. She remained at the hospital for about four weeks but was discharged as unimproved. She was observed at periodic intervals and subjected to complete physical, laboratory and roentgenologic studies. Within two months after the onset, the facial asymmetry became definite. Her condition grew progressively worse, the atrophic process continued for two years and then came to a standstill.

Examination.—On her admission to the hospital the girl was 6 years old, was rather thin and had a senile facies. The left side of the face appeared smaller than the right. There was sharp delimitation at the midline, as though the halves of the face belonged to two different persons. The tongue and nose deviated to the left. A generalized atrophy of the right lower extremity was also apparent. There were four areas of vitiligo, measuring about 1 by 2½ inches, over the left scapular region and one near the right axilla posteriorly. The hair in the left frontal region was thin, brittle and white in patches. The right knee jerk was sluggish. There were no other pathologic reflexes.

A complete blood count and differential count showed the blood to be normal. The urine was normal, and the Mantoux reaction was negative to 0.2 mg. of tuberculin. Roentgenograms showed that the chest was normal and that there were no abnormalities or atrophy of the bones and no abnormalities or calcifications of the skull. Roentgenograms taken several years later (1936) showed some atrophy of the right femur, the right tibia and the left nasal bones. (Anthropometric measurements are given in table 1.)

7. Stief, A.: Ueber einen Fall von Hemiatrophie des Gesichtes mit Sektionsbefund, Ztschr. f. d. ges. Neurol. u. Psychiat. **147**:573, 1933.

Experiments.—During the patient's stay in the hospital studies were made by Dr. A. Bell to determine the behaviour of her autonomic nervous system in response to such pharmacodynamic drugs as epinephrine, atropine and pilocarpine.

Incidentally, the experiments also throw some light on the condition of the adrenal glands, for phylogenetically the sympathetic nervous system and the chromaffin cells of the adrenal medulla have a common

TABLE 1.—*Comparative Anthropometric Measurements of a Patient with Progressive Facial and Crossed Hemiatrophy at the Age of 16 Years*

	Right Side, Cm.	Left Side, Cm.
Height of lower jaw	3.0	2.7
Length of humerus	31.8	31.8
Length of radius	24.0	23.6
Length of hand	18.8	18.8
Length of upper extremity	75.6	74.0
Length of palm	10.0	10.3
Breadth of palm	7.3	7.6
Length of femur	51.7	52.8
Length of tibia	33.6	36.0
Length of tibia (to sole)	39.8	43.6
Length of foot	24.2	26.0
Breadth of foot	8.4	8.5
Length of lower extremity	91.5	96.4
Circumference of thigh	39.2	48.6
Circumference of calf	26.7	32.4
Circumference of thorax	33.7	37.5

TABLE 2.—*Effect of Subcutaneous Injection of Epinephrine Hydrochloride on the Blood Pressure*

Time	Systolic	Diastolic
At start (2:35 p. m.)	86	58
2 minutes after start	88	50
4 minutes after start	72	50
6 minutes after start	74	52
8 minutes after start	78	58
10 minutes after start	76	58
15 minutes after start	80	58
20 minutes after start	80	58
25 minutes after start	80	58
30 minutes after start	82	50
35 minutes after start	82	58
40 minutes after start	82	58

origin. Any dysfunction of the sympathetic system must therefore result in a corresponding disturbance of the adrenal glands. The adrenal dysfunction may serve to explain a complication in our case to which we shall refer later in the report.

The experiments were conducted in the ward, which was cool and noisy. The patient was uninterested in her surroundings but cooperative. Twenty-four hour intervals were allowed between experiments.

In the first experiment, 1 cc. of a 1:1,000 solution of epinephrine hydrochloride was injected subcutaneously (table 2). The blood pressure and the pulse rate were recorded before the start, at intervals of two minutes for the first ten minutes and every five minutes for the following fifty minutes. After the injection

the blood pressure rose 30 mm. of mercury in two minutes, and the pulse rate increased 14 beats per minute with slight fluctuations. The blood pressure remained at the same high level for the next hour, while the pulse increased in frequency for the first forty minutes and then dropped several points, although it was still 40 beats per minute above normal at the end of the observations.

Comparison of these results with those given by Dresel,[8] Platz [9] and Marinesco and Sager [10] as obtained in normal controls shows a marked overactivity of the sympathetic outflow in our patient.

Twenty-four hours later 1/150 grain (0.432 mg.) of atropine sulfate was injected subcutaneously. The pulse rate with the patient lying down, standing and again lying down was first recorded. After the injection the pulse rate was taken at varying intervals, both with the recumbent and with the standing position (table 3). The size of the pupils, the condition of the throat and all other subjective alterations were recorded. The pulse rate increased from 86 to 142 a minute within ten minutes after the injection with the patient in the recumbent position and from 116 to 148 when she was in the erect position. Moreover, whereas at the start of the experiment the pulse rate returned to normal in fifteen minutes when she changed from the erect to the recumbent position, it now took only seven minutes for the pulse to return to normal when the patient assumed a recumbent posture after standing up for thirty minutes.

TABLE 3.—*Effect of Subcutaneous Injection of Atropine Sulfate on the Pulse Rate*

	Patient Lying Down	Patient Standing	Patient Lying Down Again
Time, 2:35 p. m. (at start)....	86	116	88 (15 min.)
2:40.....	100	106	120
2:45.....	142	148	144
3:20.....	146	156	156-146 (7 min.)
3:35.....	146	156	156-146 (5 min.)

When these results are compared with the data in the tables prepared by Daniélopolu and Carniol,[11] this patient is again found to belong to the sympatheticotonic group.

In addition to the alterations described, the patient complained of dryness in the mouth. She was restless and fidgety forty-five minutes after the injection, and a maximum dilatation of the pupils was observed. An hour and thirty-five minutes after the injection a red, papular rash was noted on the left side of her face, though there was no evidence of a rash on the right side.

After another twenty-four hour interval, 1/15 grain (4.32 mg.) of pilocarpine hydrochloride was injected subcutaneously. The pulse rate, the blood pressure and

8. Dresel, K.; Kraus, F., and Brugsch, T.: Speziellen Pathologie und Therapie, Berlin, Urban & Schwarzenberg, 1922, vol. 10, p. 1.

9. Platz, O.: Die pharmakologische Prüfung des vegetativen Nervensystems, Klin. Wchnschr. **30**:1413, 1923.

10. Marinesco, G., and Sager, O.: Sur la valeur des tests pharmacologiques dans l'exploration du système végétatif, Bull. de la Acad. roumaine **10**:3, 1926; Rev. neurol. **1**:513, 1926.

11. Daniélopolu, D., and Carniol, A.: Épreuves de l'atropine dans l'examen du système nerveux du cœur, Arch. d. mal. du cœur **16**:161, 1923; abstracted, J. A. M. A. **80**:1813 (June 16) 1923.

the general attitude of the patient were recorded immediately before the start of the experiment and at intervals of two minutes for the first ten minutes and at five minutes for the next fifty minutes thereafter (table 4). Interesting phenomena were observed.

The blood pressure showed a slight alteration. The pulse increased in rate, though the explanation for this acceleration is not understood. It may be stated that changes of pulse rate following the injection of pilocarpine are too irregular and varied to be of any real diagnostic value.

A prompt pilomotor reaction occurred over the entire body except in the abdominal wall on the right side and over the inner surface of the lower extremity. Contraction of the dermal smooth muscle of the skin was observed, giving the appearance of "goose flesh." This phenomenon appeared first on the left side of the body and several minutes later over the abdominal wall on the right side between the lower border of the ribs and Poupart's ligament. There was also noted sweating on the left side of the face. The right hand perspired freely; the left,

TABLE 4.—*Effects of Subcutaneous Injection of Pilocarpine Hydrochloride*

Time	Blood Pressure	Pulse Rate
At start (2:35 p. m.)	102	80
2 minutes later	94	92
4 minutes later	100	90
6 minutes later	100	96
8 minutes later	106	104
10 minutes later	106	106
15 minutes later	106	104
20 minutes later	106	100
25 minutes later	106	100
30 minutes later	106	106
35 minutes later	104	106
40 minutes later	102	106
45 minutes later	102	96
50 minutes later	98	96
55 minutes later	106	114

very little. Urination occurred twelve minutes after the experiment began, and vomiting three or four times at the end.

We are fully aware of the limitations of the experiments which we made, especially since the results obtained with pilocarpine and atropine, are qualitative rather than quantitative. We also appreciate the difficulty of obtaining accurate descriptions of subjective states from a 6 year old child; yet the conditions observed appear significant enough to warrant the conclusion that our patient is suffering from an absolute or relative hypertonus of the autonomic nervous system. It was suggested by Dr. Bell on the basis of these experiments that the disease is most likely due to a toxic degeneration of the trophic centers in the midbrain in an already predisposed, poorly endowed nervous system.

Subsequent Course.—Several days after the completion of these experiments the patient was discharged as unimproved. Since that time she has been observed at periodic intervals in the examining room of the outpatient department. On successive visits it was noted that the atrophy and resultant asymmetry became more marked. The mandible appeared to consist of two parts differing strikingly

as to form and dimensions. The left side was shorter and thinner than the right. The left labial angle approximated the eye more closely than the one on the opposite side. The distance between the right labial angle and the right nostril

Fig. 1.—Hemiatrophy of the face (left side). There is deviation of the nose to the left, and patches of gray hair may be seen in the frontal region.

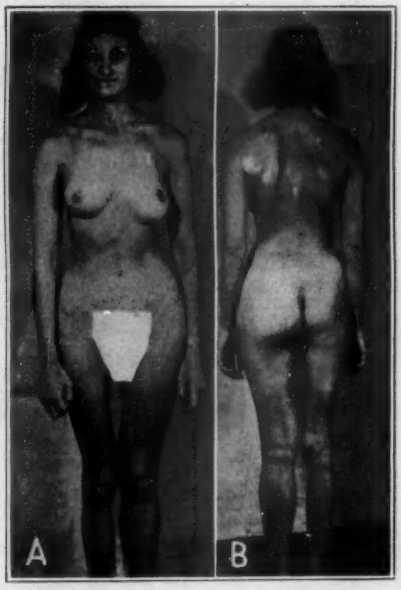

Fig. 2.—Crossed hemiatrophy. *A*, anterior view, showing hemiatrophy of the left side of the face and of the right side of the body. *B*, posterior view, showing several areas of vitiligo over the scapular region.

was greater than the corresponding distance on the left side. The entire left side of the face was appreciably smaller than the right side, especially in the region of the cheek. The wrinkles on the forehead were diffierent on the two sides as to shape and form. The left orbit was diminished in size, and the left supraorbital ridge

Fig. 3.—View of both hands. Note the atrophy of the right palm.

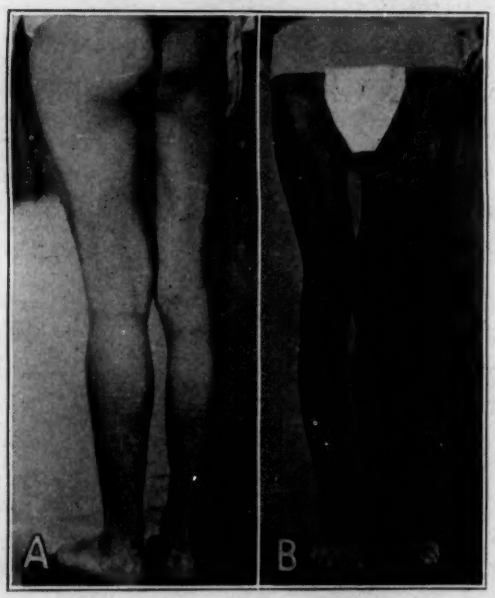

Fig. 4.—*A*, view of the buttocks and legs, showing marked atrophy of the right side. *B*, view of thighs and legs.

appeared narrower than the right. There were also a narrowing of the left palpebral fissure and enophthalmos on the same side.

The left nostril and the left ear appeared slightly smaller than the corresponding structure on the right side. No marked atrophy of the upper extremities could be seen. The right lower extremity was noticeably atrophied, and there was also an extensive atrophy of the right buttock. The thorax showed a marked

asymmetry, the right side having developed much less than the left. The right breast was smaller than the left, and the circumference from the midspine to the midsternum on the right side was greatly diminished in size. The left side of the tongue was thinner than the right, and the organ deviated to the left. The teeth did not show any asymmetry, and the palate appeared equal on the two sides.

Three years after the onset of the disease, the patient began to complain of dizziness and of feeling as though she were going to faint. The condition was particularly precipitated in the presence of any odor. She fainted once after smelling some medicine in a bottle. At no time did the patient bite her tongue during an attack, nor was there any aura associated with the fainting-like episodes. An attack usually lasted several minutes. Two years after the initial attack she fainted in a church, and she attributed this attack to heat exhaustion. The patient states that she invariably has an attack after taking a cathartic. Up to date she remembers having about eleven attacks similar in nature. There is no history of tonic or clonic convulsions or of epileptiform seizures. About two years ago, after a toothache, she consulted a dentist. During the injection of procaine hydrochloride and before the extraction was even begun she fainted in the dentist's chair. This attack is said to have lasted about fifteen minutes.

Five years ago, after the completion of a prolonged and detailed physical examination, including roentgenologic and anthropometric studies, blood was drawn from a vein in the arm for the purpose of chemical analysis. Several minutes later the child was covered with perspiration and fainted. The pulse was rapid but shallow, the skin clammy and cold. The episode lasted about five minutes and was followed by spontaneous recovery, after which the patient went home. Examination of the blood drawn showed a sugar content of 35 mg. per hundred cubic centimeters. The other constituents were all within normal limits.

About two years ago, after a similarly prolonged examination, including a photographic study, the patient complained of feeling dizzy while she stood before the camera. She was immediately put on an examining table. The pulse rate as well as the skin presented conditions almost identical with those observed during the previously described episode. The juice of two oranges was promptly administered, and the patient recovered without fainting. Blood was then drawn from a vein, and a determination of the sugar content showed 69 mg. per hundred cubic centimeters. The other components were again within normal limits.

It is recognized that on both occasions the blood sugar was decidedly below normal, showing a definite hypoglycemia.

The patient does not suffer from headaches nor from recurrent vomiting. She has no history of any attacks simulating epileptiform seizures. Her major complaint is an inability to gain weight in spite of a good appetite. When seen recently, on April 14, 1939, she appeared in high spirits. She is extremely cooperative and intelligent. In spite of her facial and bodily disfiguration she is socially well adjusted. At present she is a freshman in college, has joined several societies, is a member of the fencing team and is also active in swimming. Her memory is said to be excellent for past events but not good for recent ones, especially those involving many details.

The patient perceives no difference in sensation on the two sides, although for the past few months she has observed a loss of sensation over the plantar surface of the large toe of the right foot, whereas the dorsal surface of the same toe appears hypersensitive. She also has complained of being unable to stand for any prolonged time on her right heel.

Occasionally she experiences "stinging pains" in the epigastrium, as though "something were moving around."

As previously stated, the atrophic process came to a standstill within three years, and for the past seven years it has been stationary. When last examined, on April 14, 1939, she presented essentially the same conditions as those already described.

COMMENT

The syndrome under consideration here was first described by Moritz Heinrich Romberg in 1846. Elenberg, however, was the first to name it progressive facial hemiatrophy.

In 1932, Archambault and Fromm [5] wrote an excellent and extensive article on this clinical entity, reviewing the literature up to that time, which comprised reports of about 365 cases. Merritt, Faber and Bruch [2] reviewed the literature from 1932 to 1936, bringing the total number of cases to about 400. Since that time several additional cases have been reported.

Although the exact etiology and pathogenesis of this syndrome are still obscure, there is sufficient clinical evidence based on the symptoms, especially the strict midline demarcation, to indicate that it is of neurogenic origin. We do not agree, however, with Archambault and Fromm,[5] Stief [7] and others that it is due to a disturbance of the sympathetic nervous system alone.

Though the many symptoms and results of clinical studies with pharmacodynamic drugs, as shown in our patient, point to a derangement of the sympathetic nervous system, it must be remembered that these studies are subject to many variations and consequently have their limitations. One must be extremely careful in drawing conclusions from pharmacologic observations even on normal persons. Certain so-called specific sympathetic or parasympathetic drugs, while presumably antagonistic in their action, may at times act on both systems in a similar manner. Their action will depend on the chemical conditions in the periphery, which influence the excitability of the nervous end apparatus. There is sufficient clinical and experimental evidence [12] to indicate that the excitability of the sympathetic nervous system is increased if the acid-base balance in the blood is shifted toward the alkaline side and that the excitability of the parasympathetic system is increased if the balance is shifted toward the acid side.

Roberts [13] showed that epinephrine, though a stimulator, has an inhibitory effect on the respiratory center. Cushing [14] likewise showed

12. Speigel, E. A.: The Autonomic Nervous System, in Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1937, vol. 4, chap. 5, p. 19.

13. Roberts, F.: The Effect of Adrenalin upon Respiration, J. Physiol. **55**:346, 1921.

14. Cushing, H.: Similarity in Response to Posterior Lobe Extract (Pituitrin), and to Pilocarpine When Injected into Cerebral Ventricles, Proc. Nat. Acad. Sc. **17**:171, 1931.

a central action for pilocarpine by injecting into the cerebral ventricles small doses of this drug which are ineffective if injected subcutaneously. The effect was vasodilatation, sweating, vomiting and lowering of body temperature. In addition, the sympathetic nervous system is extremely unstable, and some of the end results may rightly be attributed to the toxicity of the drug.

Trophic disturbances occur usually as a result of inactivity, vascular and endocrine disturbances where there is a loss of protective reflexes. The clinical entity present in our case, however, does not fall in the categories just described. The syndrome is a puzzling one indeed. It may not be amiss to quote here a notation made by Dr. Foster Kennedy when he first saw our patient on Dec. 10, 1926, twelve and a half years ago:

"Premature senility, leukoderma, left facial hemiatrophy, generalized atrophy of the right lower extremity.—I have been struck by the retention of youth in persons suffering from pituitary tumors. One remembers that Fröhlich's syndrome produces an appearance of childhood in the adult. I am forced to believe that this child suffers a grave endocrine error, perhaps in the field of hyperpituitarism and adrenal lack. If we can solve her problem we shall be as the gods."

Dr. Kennedy brings up the question of Fröhlich's syndrome and adrenal lack. There certainly must be a deficiency of the adrenal medulla in these cases, for the chromaffin cells in the adrenal medulla are of sympathetic origin.

It has been observed that destruction of the hypothalamus and a tumor of the base of the brain without associated injury to the hypophysis may produce a clinical entity entirely indistinguishable from Fröhlich's syndrome, and many examples of so-called Fröhlich's syndrome are believed to be due to a lesion of the hypothalamus. Carrying this observation a step further, we believe it is logical to assume that a syndrome presenting the opposite clinical manifestations from those seen in Fröhlich's, i. e., senility and marked undernutrition, may arise from a lesion in the same organ, namely, the hypothalamic area, the pons or the midbrain. Numerous observers in order to explain the mechanism of progressive facial hemiatrophy assume the existence of specific centers and nerves, and some believe that the sympathetic nerve endings in the skeletal muscles have this trophic function. However, the existence of these centers and nerves has never been demonstrated anatomically or clinically. They therefore belong to the realm of suppositions and conjectures. On the contrary, one remembers that sympathectomy does not as a rule result in muscular atrophy. Also it is known that unilateral lesions of the autonomic centers produce bilateral effects peripherally, though more marked on one side than on the other.

It is thus difficult to believe that this syndrome is a result of a lesion of the sympathetic nervous system only, especially when the atrophy is not limited to the face but involves the entire half of the body or, rarer still, when, as in our patient, there is an alternate atrophy, implying a decussation of fibers. That there is a close functional relation between the endocrine glands and the nervous system is well known. The endocrine glands affect and are in turn influenced by the nervous system. The sharp midline demarcation of this syndrome, however, points conclusively to a primary nervous disorder rather than to an endocrine dysfunction.

We believe, therefore, that the disease in all probability results from a toxic or infectious process, causing a degeneration of the central nervous system in the hypothalamus, pons or midbrain and involving also the sympathetic and parasympathetic fibers.

The hypoglycemia seen in our patient may be caused either by the adrenal lack, i. e., by a diminished output of epinephrine which in turn produces a fall in the blood sugar level, or by a hypersecretion of insulin, occurring as a result of a vagal stimulation of the pancreas.

TREATMENT

There is no known specific form of therapy. In the light of the present knowledge of the action of vitamins, it seems to us that if this syndrome is recognized early massive doses of thiamin chloride may prove beneficial, especially if given at the onset of the disease. We could find no reference to this treatment in the literature on facial hemiatrophy.

Moszkowicz,[15] Eitner [16] and others suggested a plastic operation by means of fat transplants. Considerable cosmetic improvement has been obtained in severe cases of facial disfigurement with this form of therapy. Moszkowicz employs a flap of fat connected with the fascia lata for the purpose of padding the skin of the face. The pad is cut into long narrow strips and stuffed through a small incision underneath the skin of the cheek by means of a trocar. Eitner uses a flap of fat about the size of a child's fist from the hypogastric region. This flap is inserted underneath the skin of the cheek through an incision in the skin. In this manner an overcorrection which may at first appear even more striking than the original defect is achieved. Several months after the operation the overcorrection diminishes in size and assumes normal proportions, filling out the previously atrophied face in an almost perfect manner.

15. Moszkowicz, L.: Fettplastik bei Hemiatrophia faciei, Med. Klin. **26**:1478, 1930.

16. Eitner, E.: Fettplastik bei Gesichtsatrophie, Med. Klin. **17**:623, 1931.

SUMMARY

A case of facial and crossed hemiatrophy complicated by hypoglycemia is here reported. An attack of measles is believed to have been the inciting factor.

The pathogenesis of this clinical entity is still obscure, but the mode of production must be varied. The syndrome possibly is caused by a degeneration of the central nervous system in the hypothalamus or midbrain and involving also the autonomic nervous system.

An explanation for the hypoglycemia is offered, and forms of treatment are mentioned.

Progress in Pediatrics

A CLINICAL STUDY OF TETANUS

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During the early part of the summer of 1932, 3 fatal cases of tetanus in children were observed within a relatively short time. The routine treatment of the patients and of those hospitalized previously had consisted of general ward care, antitoxin administered by the intrathecal route in combination with other routes, emphasis on radical surgical care of the local lesions and variable degrees of attention to sedative therapy. On the suggestion of the staff of the Children's Hospital, I decided to reinvestigate the subject of tetanus in the hope that the treatment might be improved. This presentation gives the results of my study and of the application of certain newer therapeutic measures in the management of 33 patients with tetanus. Table 1 summarizes the significant data of this series. Included as a basis for comparison is a discussion of the observations made on an equal number of patients treated according to the older methods. Three of this group were treated after 1932, but not in strict accordance with the newer routine.

SEDATIVE THERAPY

Analysis of the results obtained in this institution prior to 1932 in the cases of 30 patients treated by the then customary methods indicated that any reduction in the case fatality rate would require more effective control of convulsions. Among 14 patients without convulsions only 1 death occurred, whereas 9 of 16 patients with convulsions died.

Although a dark, quiet environment and the employment of measures designed to increase the patient's comfort are of considerable aid in preventing tetanic spasms, chief reliance must be placed on active sedative therapy. The prognostic importance of both the intensity and the frequency of convulsions justifies primary emphasis on this phase of treatment. Mild tetanus may be encountered in patients free from convulsions, moderately severe tetanus in patients without cyanosis during tetanic spasms and severe tetanus in patients with cyanosis as a prominent feature of the typical convulsive seizure. Spasms associated

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with cyanosis and dyspnea may cause asphyxia and sudden death. Those unaccompanied by these signs may occasion marked discomfort and profound exhaustion but do not lead to sudden death. Either type of convulsion may facilitate the development of aspiration pneumonia or may cause compression fractures of the vertebrae.[1] For these reasons, rigidity and convulsions must be controlled by keeping the patient in a state of light to moderate narcosis until convalescence is definitely established. Such a program may require the employment of sedative drugs for two or more weeks. Minimal effective doses are desirable, in order to avoid depression of the cough reflex and the resultant danger of aspiration pneumonia.

The more severe the tetanus, the greater is the limitation in the choice of sedatives, and for the acute fulminating condition no drug may be satisfactory. Of the many depressant drugs recommended in the literature, avertin with amylene hydrate (tribromethanol dissolved in amylene hydrate)[2] and sodium amytal (sodium isoamylethylbarbitu-

1. Dietrich, H. F.: Tetanus in Childhood, Am. J. Dis. Child. **59**:693-710 (April) 1940.

2. (*a*) Anschutz, W.; Specht, K., and Tiemann, F.: Die Avertinnarkosen in der Chirurgie, Berlin, Julius Springer, 1930, pp. 582-586. (*b*) Bernheim, M. J.: Avertin Used in the Treatment of Tetanus, Anesth. & Analg. **16**:333-336 (Nov.-Dec.) 1937. (*c*) Boyce, F. F., and McFetridge, E. M.: The Rationale of the Therapy of Tetanus with Especial Reference to Avertin, Internat. S. Digest **19**:131-144 (March) 1935. (*d*) Bradshaw, P. S.: Tetanus Treated Successfully by Antitoxin, Avertin, and Respirator, Am. J. Dis. Child. **49**:1373-1374 (May) 1935. (*e*) Bromeis: Die Avertinbehaundlung des Wundstarrkrampfes, München. med. Wchnschr. **78**:2063 (Nov. 27) 1931. (*f*) Drost, E., and Buzello, A.: Ueber die symptomatische Behandlung des Tetanus mit Avertin, Beitr. z. klin. Chir. **155**:311-320, 1932. (*g*) Cole, L.: Treatment of Tetanus, Brit. M. J. **1**:1191-1195 (June 13) 1936. (*h*) Chia, F. W.: The Treatment of Tetanus by Cole's Method, Chinese M. J. **54**:70-71 (July) 1938. (*i*) Fawcett, A. W.: Avertin for Tetanus Convulsions, Brit. M. J. **1**:1171 (June 8) 1935. (*j*) Freeman, E. T.: Observations on Treatment of Tetanus, Irish J. M. Sc., April 1936, pp. 166-170. (*k*) Gage, M., and DeBakey, M.: Tetanus and Its Treatment, Am. J. Surg. **30**:157-167 (Oct.) 1935. (*l*) Gerbatsch: Avertin und Pernocton bei einem Tetansulfall, Zentralbl. f. Chir. **58**:563-565 (Feb. 28) 1931. (*m*) Harrison, F. A.: Three Cases of Tetanus: Treatment with Antitoxin, Controlled by Avertin, Am. J. Dis. Child. **45**:445-446 (Feb.) 1933. (*n*) Hempel, C.: Weitere Erfahrungen über die Behandlung des Tetanus mit hohen Dosen spezifischen Serums in Avertinnarkose, Arch. f. klin. Chir. **185**:373-376, 1937. (*o*) Herbrand, J.: Avertinbehandlung bei Tetanus, München. med. Wchnschr. **79**:957-959 (June 10) 1932. (*p*) Huntington, R. W., Jr.: The Treatment of Tetanus, Yale J. Biol. & Med. **3**:207-233 (Jan.) 1931. (*q*) Jeans, P. C.: Treatment of Tetanus, cited by Davison, W. C.: The Compleat Pediatrician, Durham, N. C., Duke University Press, 1938. (*r*) Knop, F.: Avertin zur Behandlung des Tetanus, München. med. Wchnschr. **77**:184 (Jan. 31) 1930. (*s*) Läwen, A.: Avertin zur Behandlung

(Footnote continued on page 136)

TABLE 1.—*Summary of Thirty-Three Cases of Tetanus Treated At Iowa University Hospital from May 1933 to June 1938*

Case	Age	Hospitalization	Symptoms	Incubation Period, Days	Day of Disease Given Serum	Lesion		Treatment of Local Lesion		Antitoxin Therapy,* Thousands of Units	Day of Delayed Serum Reaction †	Sedatives	Complications	Recovery or Death
						History	Observation	Prior to Hospitalization	In Hospital					
1	4	5/17 to 6/18/33	Severe	20	2	Vaccination wound infected in barn	Infected vaccination wound	None	Excision of lesion (ethylene anesthesia)	60	11	Avertin with amylene hydrate, sodium amytal	.....	R
2	11	7/5 to 7/20/33	Moderate	14	4	Splinter in left ankle	Small splinter wound	None	Excision of wound	60	7	Avertin with amylene hydrate, sodium amytal	.....	R
3	3	7/6 to 8/1/33	Severe	3	2	Stepped on a nail	Healed puncture wound on left sole	Tincture of iodine	None	80	10	Avertin with amylene hydrate	.....	R
4	5	7/23 to 8/1/33	Mild	?	6	None	None	.....	.....	20	7	Avertin with amylene hydrate	.....	R
5	32	8/5 to 8/17/33	Moderate	7	1	Lye burn of leg	Lye burn of leg	Milk and soda	Butesin picrate dressings	60	5	Avertin with amylene hydrate, sodium amytal, soluble phenobarbital U. S. P.	.....	R
6	13	9/1 to 10/3/33	Moderate	6	1	Splinter from plow entered hand	Abscess of palm of hand	Tincture of iodine; hot compresses; removal of splinter	Abscess drained; splinter removed; wound irrigated	30	5	Avertin with amylene hydrate	Otitis media	R
7	9	6/16 to 6/26/34	Mild	8	3	Stepped on a rusty nail	Healed puncture wound	Foot cleansed with turpentine	None	15	2 §	Avertin with amylene hydrate, sodium amytal	.....	R
8	10	8/8 to 8/14/33	Mild	?	6	None	Healed puncture wounds of both soles	None	None	20	..	Avertin with amylene hydrate	.....	R
9	2½	6/13 to 6/20/34	Mild	?	6	Pebbles in nose ?	None	None	None	10	..	Avertin with amylene hydrate, sodium amytal	.....	R

10	9	8/29 to 9/23/34	Moderate	8	1	Chicken bone penetrated foot	Healed puncture wound of heel	Removal of chicken bone; hot dressings	Removal of chicken bone; drainage of pus	20	..	Avertin with amylene hydrate, sodium amytal, soluble phenobarbital U. S. P.	.....	R
11	11	7/13 to 8/14/35	Moderate	7	6	Cut left sole while playing outdoors	Small puncture wound on sole	Cleansed with salt water and lysol	Splinter removed; drainage of pus	60	5	Avertin with amylene hydrate, sodium amytal	.....	R
12	9	8/22 to 9/3/35	Moderate	7	1	Stepped on a nutshell	Small localized infection of foot	Occasional dressing	Not recorded	60	6	Avertin with amylene hydrate, sodium amytal	.....	R
13	4	11/8 to 12/3/35	Mild	?	6	Burn of finger; cut of finger	Healed burn of arm; small scab on middle finger of right hand	None	None	11	..	Sodium amytal, soluble phenobarbital U. S. P.	Hallucinosis	R
14	14	7/28 to 8/6/36	Mild	3½	1	Stepped on a nail in barnyard	Small inconspicuous puncture wound on bottom of foot	Bathed foot; tincture of iodine	Incised wound; tincture of iodine pack	60	4	Avertin with amylene hydrate, sodium amytal	.....	R
15	13	8/3 to 8/18/36	Moderate	5-6	5	Ran ice pick through finger	Puncture wound of finger	None	None	40	8	Avertin with amylene hydrate, sodium amytal	.....	R
16	11	8/20 to 9/5/36	Moderate	28	4	Scraped hand against gravel	Small healed scars on palm of hand	Gravel removed from hand a few days after accident	None	60	6	Avertin with amylene hydrate, sodium amytal	.....	R
17	4	9/11 to 9/29/36	Severe	?	2-3	Cut foot on cocklebur	Number of old healed scars on feet	None	None	60	..	Avertin with amylene hydrate, sodium amytal	Pneumonia	R
18	12	5/20 to 6/16/37	Moderate	10	3	Scratched right thigh on dry weed	Two infected abrasions of right thigh	Wound squeezed by local physician	Drainage of pus	60	10	Avertin with amylene hydrate, sodium amytal	Diabetes mellitus	R
19	7	7/5 to 7/18/37	Moderate	?	7	Splinter in foot; went barefoot	Pustular lesion on left heel	None	Drainage of pus; removal of splinter	62.5‡	6	Avertin with amylene hydrate, sodium amytal	.....	R
20	6	9/19 to 10/6/37	Severe	?	6	Scratch on foot	Clean scratch on foot	None	None	60	..	Sodium amytal	.....	R

TABLE 1.—*Summary of Thirty-Three Cases of Tetanus Treated At Iowa University Hospital from May 1933 to June 1938—Continued*

Case	Age	Hospitalization	Symptoms	Incubation Period, Days	Day of Disease Given Serum	Lesion		Treatment of Local Lesion		Antitoxin Therapy,* Thousands of Units	Day of Delayed Serum Reaction †	Sedatives	Complications	Recovery or Death
						History	Observation	Prior to Hospitalization	In Hospital					
21	35	11/14 to 12/20/37	Moderate	60	2	Splinter in finger	Swelling and tenderness of right middle finger with drainage, axillary and epitrochlear glands inflamed	Two incisions by physician; removal of fingernail	Amputation of middle finger; incision of wrist and forearm because of apparent gas gangrene	60	..	Avertin with amylene hydrate	Gas gangrene	R
22	3	6/3 to 6/19/38	Severe	14	4	Splinter in bottom of foot	Pinpoint wound with some pus on ball of right foot; no redness or swelling	Mother removed two splinters; druggist applied salve	None recorded	40	10	Avertin with amylene hydrate, sodium amytal	Pneumonia	R
23	57	9/14 to 9/21/38	Moderate	8	2	Stepped on "snag of weed" in cowpasture	Small puncture wound with pus on left foot between toes	Wound dressed by local physician	Débridement of wound; removal of weed, 3 cm in length	60	..	Avertin with amylene hydrate	Pneumonia; retention of urine	R
24	4	7/18 to 7/30/38	Mild	?	5	None	None	.....	.....	40	9	Avertin with amylene hydrate, sodium amytal	Otitis media	R
25	15	6/29 to 7/1/34	Severe	5	1	Stepped on a nail	Puncture wound on sole of foot	None	Blister in foot opened	20	..	Avertin with amylene hydrate, sodium amytal	Pneumonia	D
26	13	7/15 to 7/16/36	Moderate	10	2	Fourth of July injury (0.22 blank cartridge shot of hand)	Puncture wound with secondary infection of hypothenar eminence	Wound dressed by local physician	Wound cauterized with phenol; wad of blank cartridge shell removed; peroxide packs placed in wound	60	..	Avertin with amylene hydrate	Pneumonia	D
27	9	7/31 to 8/2/36	Severe	5	4	Splinter from railroad track entered bottom of left foot	Several clean scars on sole of left foot	Mother removed splinter and applied mercurochrome	All questionable lesions explored surgically	60	..	Avertin with amylene hydrate	Pneumonia	D
28	9	6/9 to 6/12/37	Severe	6	1	Probably abrasions on ball of right foot	Both healed and infected abrasions on ball of right foot	Wound bandaged; hot water bottle over wound	Sterile dressings	40	..	Avertin with amylene hydrate, sodium amytal	Pneumonia	D

29	14	6/20 to 6/21/37	Severe	5	1	Stepped on rusty nail in barn	Short incision on ball of right foot; packed with gauze	Father incised foot and packed with gauze; parents applied mercurochrome and bread and butter poultice; physician incised foot day before hospitalization	None	82	..	Avertin with amylene hydrate, sodium amytal	Pneumonia	D
30	9	7/31 to 8/5/37	Severe	?	1	None	Many scratches over soles of feet; sliver removed at autopsy from tissue over left external malleolus	None	None	60	..	Avertin with amylene hydrate	Pneumonia	D
31	4	8/12 to 8/14/37	Severe	5	2	Stepped on a nail	Scars on soles; healed puncture wound on sole of right foot	None	None	60	..	Avertin with amylene hydrate	Pneumonia	D
32	13	6/3 to 6/6/38	Severe	6	1	Stepped on a rusty nail	Small healed puncture wound on sole of left foot	Foot cleansed with soap and water; mercurochrome; father probed with needle and poured whisky over wound	None	60	..	Avertin with amylene hydrate	Pneumonia; congenital left hydronephrosis	D
33	6	7/8 to 7/18/38	Severe	6	1	Stepped on a rusty nail	None found	None	None	Amount not stated	7	Avertin with amylene hydrate, sodium amytal	Pneumonia	D

Classification of symptoms: mild, convulsions absent; moderate, convulsions without cyanosis; severe, convulsions with cyanosis.

All patients were white. All were males except in the following cases: 2, 5, 16, 21 and 28.

* All antitoxin expressed in units given as single dose by vein during the first twenty-four hours of hospitalization, except as otherwise indicated.

† Expressed in terms of days after injection of therapeutic serum.

§ Twelfth day after injection of a prophylactic dose of 1,500 units of antitoxin.

‡ 2,500 units injected about the wound.

rate) [3] have proved to be fairly reliable for routine use. In the average case of tetanus these drugs have effected prompt and satisfactory control of the neuromuscular manifestations of the disease, with a minimal degree of risk because of their relatively wide margins of safety.[4]

The response to sedative drugs is an excellent indicator of the degree of excitation in the central nervous system and is therefore of great prognostic aid. For these reasons it is desirable to make twenty-four hour summaries of the quantities of the depressant drug required. Prompt and satisfactory induction of relaxation with amounts which cause only minimal loss of consciousness points toward a mild to

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des Tetanus, Zentralbl. f. Chir. **54**:2370-2377 (Sept. 17) 1927; Weitere Erfahrungen über die symptomatische Behandlung des Tetanus mit Avertin, ibid. **55**:194-201 (Jan. 28) 1928. (*t*) Lindemann, K.: Zur Anwendung des Avertin beim Wundstarrkrampf, ibid. **56**:1282-1284 (May 25) 1929. (*u*) Loewe, G.: Zur Behandlung des Wundstarrkrampfes mit Avertin, Deutsche Ztschr. f. Chir. **235**:814-819, 1932. (*v*) Mitchell, H. S.: Avertin as an Auxiliary Therapeutic Measure in Tetanus, Canad. M. A. J. **32**:415-417 (April) 1935. (*w*) Melzner, E.: Experimentelle Untersuchungen über die Behandlung des Wundstarrkrampfes mit einer Kombination von Curarin und Avertin, Deutsche Ztschr. f. Chir. **212**:308-324, 1928. (*x*) Momburg, F., and Rotthaus, E.: Avertindosierung. Avertin bei Tetanus, Deutsche med. Wchnschr. **55**:1164-1165 (July 12) 1929. (*y*) Obladen, E.: Ueber die Avertinbehandlung des Wundstarrkrampfes. Unter Berücksichtigung von 17 Fällen der Heidelberger chirurgischen Universitätsklinik, Chirurg **10**:155-159 (March 1) 1938. (*z*) Schamoni, H.: Avertin- und Pernoctonanwendung beim Wundstarrkrampf, Zentralbl. f. Chir. **57**:1408-1411 (June 7) 1930. (*a'*) Seifert, E.: Avertin bei Tetanus, München. med. Wchnschr. **79**:697 (April 22) 1932. (*b'*) Spaeth, R.: Treatment of Tetanus, Am. J. Dis. Child. **48**:467-468 (Aug.) 1934. (*c'*) Teichmann, T.: Die Avertinnarkose beim Tetanus, München. med. Wchnschr. **79**:135-137 (Jan. 22) 1932. (*d'*) Wolf, A.: Avertin bei Wundstarrkrampf, Zentralbl. f. Chir. **56**:2200-2202 (Aug. 31) 1929. (*e'*) Wiedkopf, O.: Behandlung des Wundstarrkrampfes mit grössen Intravenösen Heilserumsgaben, Deutsche Ztschr. f. Chir. **232**:105-112, 1931.

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moderate degree of neuromuscular irritation. In contrast, the condition is to be considered severe if the quantities needed lead to marked cerebral depression. If convulsions persist despite intensive sedative therapy, the outlook becomes particularly grave.

Both the nurses and the medical attendants should be carefully instructed in the administration of sedative drugs in the presence of definite indications, namely, restlessness, significant rigidity of the skeletal muscles (neck, abdomen, trunk or extremities) or tonic spasms. When cyanosis accompanies convulsions it is of the greatest importance to determine whether the respiratory difficulty is occasioned by the spasms themselves or by obstruction of the nasopharynx with secretions which cannot be swallowed. If the latter can be incriminated, the indication is for removal of the secretions and for conservative, rather than intensive, sedative therapy.

To expedite treatment, printed outlines are invaluable. On these routine forms, in addition to the data usually recorded, the weight of the patient should be stated in order to insure accuracy in the calculation of schedules of dosage for the various sedative drugs. Information should be noted concerning any previous medication or drug sensitivity, because sodium amytal should be administered very cautiously, if at all, after administration of morphine and to patients known to be especially sensitive to this or related drugs. Idiosyncrasy to sodium amytal must be determined by questioning about or by detecting the occurrence of cutaneous reactions, speech disorders, diplopia, ataxia and mild states of confusion, delirium or stupor following the use of the drug. Obviously, any of the mental aberrations mentioned might introduce diagnostic confusion, because the mind is clear in cases of uncomplicated tetanus. A record of the age, blood pressure, general condition and other diseases or complications is essential for the reason that both intravenous and intramuscular injections of sodium amytal are best avoided in the cases of elderly patients and of those with either elevated or depressed blood pressure, generalized arteriosclerosis, edema, cachexia of any degree, acidosis or obesity. Furthermore, sodium amytal might possibly be considered as a substitute for avertin with amylene hydrate if the patient shows evidence of significant hepatic or bilateral renal disease. On the latter point, however, there is a definite difference of opinion.[5]

A table should be prepared for each patient to indicate the number of cubic centimeters of 2.5 per cent solution of avertin with amylene

5. Dreyer, N. B.; Brueger, M., and Bourne, W.: Effects of Avertin on Liver Function, Am. J. Surg. **9**:82-87 (July) 1930. Dandy, W. E.: "Avertin" Anesthesia in Neurologic Surgery, J. A. M. A. **96**:1860-1862 (May 30) 1931. Waters and Muehlberger.[4a]

hydrate corresponding to 100, 50, 25, 15 and 10 mg. of tribromethanol per kilogram of body weight. The amount of sodium amytal equivalent to 5 mg. per kilogram of body weight should be expressed in milligrams, grains and cubic centimeters of 5, 10 and 20 per cent solutions respectively.

I consider avertin with amylene hydrate an excellent preparation for general use. When given in the form of a retention enema, with distilled water, this drug causes prompt depression in the central nervous system because of the rapid absorption of the tribromethanol, at least half of which is removed from the watery menstruum within ten minutes and about three fourths in approximately twice that time.[6] Control of spasms and the appearance of muscular relaxation ordinarily follow within five to ten minutes if adequate doses of the drug are employed. These features make the drug available to those not skilled in parenteral methods of therapy. The trauma and excitement caused by hypodermic medication are avoided. A stock solution of appropriate concentration may be adapted readily to the variable requirements imposed by age, weight and the intensity of specific signs and symptoms. For this reason, any number of patients may be treated with a given stock solution. Ordinarily a fairly constant level of narcosis may be maintained by keeping the patient in a state of light to deep depression. It is to be emphasized, however, that a definite routine must be followed if avertin with amylene hydrate is to be employed both safely and effectively. For the average patient with tetanus the initial dose may be an amount providing 25 mg. of tribromethanol per kilogram of body weight, to be followed at fifteen to thirty minute intervals with 10 to 15 mg. per kilogram, according to the requirements of the individual patient. This initial dose may be increased to 40 or 50 mg. per kilogram if severe asphyxial spasms are present, or it may be reduced to 15 mg. per kilogram if convulsions are absent. A liberal excess of stock solution, already diluted, should be available at all times. The rectal tube should be left in place as much as possible so that avertin with amylene hydrate may be administered without delay in the event of acute asphyxial spasms. Although aqueous solutions of tribromethanol are stable at room temperature for twenty-four to forty-eight hours,[4a] the material should be tested with congo red before each administration of the drug. The appearance of a blue or violet color indicates the presence of a toxic dibromacetaldehyde, caused either by aging or by preparation of the solution with excessively hot

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6 (*a*) Straub, W.: Rektalnarkose mit Avertin (Resorption und Dosierung), München. med. Wchnschr. **75**:593-595 (April 6) 1928. (*b*) Schlaepfer, K., and Peters, L. M.: Avertin Fluid Anesthesia in Surgery, Arch. Surg. **24**:868-879 (May) 1932. (*c*) Waters and Muehlberger.[4a] Sollmann,[4c] p. 715.

water. Such material is unfit for further use. This test with congo red is reliable only when distilled water has been used as the diluent.

Sodium amytal may be used alone or in conjunction with avertin with amylene hydrate. In the presence of rectal irritation or incontinence and possibly of renal or hepatic disorders, sodium amytal may be preferable to the latter drug. Sodium amytal may be given by any of the available channels of therapy, whereas avertin with amylene hydrate can be administered only by rectum. According to my experience, the routine initial dose of sodium amytal can safely be calculated on the basis of 5 mg. per kilogram of body weight, with an upper limit of 240 mg. for children and of 480 mg. for adults. If conditions permit, it is desirable to use single injections not exceeding the former value, independent of the age of the patient. For the average patient with tetanus the intramuscular injection of a 10 per cent aqueous solution may be employed. If the dose exceeds 256 mg., a 20 per cent solution may be used to reduce the volume of the injection. Further injections may be given at thirty to sixty minute intervals when indicated. The amounts required may be judged by the response to the initial dose. The narcosis induced by intramuscular therapy is both slower in its development and less profound than is that following intravenous medication. Resort to the intravenous channel is justified only in the presence of severe asphyxial spasms. A solution containing preferably only 5 per cent and not over 10 per cent of sodium amytal in sterile distilled water should be injected at a rate of only 1 cc. per minute. It is essential that the injection be accurately timed, because more rapid administration of the drug may cause profound overdepression, central respiratory arrest or dangerous drops in blood pressure. The sedative action becomes apparent during the intravenous injection, and treatment may be discontinued as soon as relaxation or sleep begins to appear. The calculated dose of sodium amytal may be given orally, dissolved in orange juice or some other pleasant vehicle, if difficulty in swallowing is absent and no acute emergency exists. The rectal route may be used when rapid action is not essential in the case of a patient unable to swallow and with conditions which contraindicate injection by muscle or by vein. The effects from oral or rectal administration of the drug are relatively slow but usually are complete within thirty to forty-five minutes.

Table 2 summarizes the sedative therapy employed for 19 patients of the new series.

Clinical evidences of toxic injury to body organs did not appear after the administration of large amounts of avertin with amylene hydrate or of sodium amytal to those patients who recovered. These findings are in

accord with the reported observations of others.[7] In agreement with previous investigations,[8] states of acquired resistance to either drug were not encountered in my patients. However, 2 patients (cases 30 and 31) had repeated spasms despite massive doses of avertin with amylene hydrate. The fact that respiratory depression or profound vasomotor collapse may follow single large doses of either avertin with amylene hydrate or sodium amytal makes fractional administration essential. The patient in case 14 had cyanosis, shallow respirations and a temperature of 103 F. after an initial dose of avertin with amylene hydrate

TABLE 2.—*Summary of Avertin with Amylene Hydrate and Sodium Amytal Therapy*

			Tribromethanol					Sodium Amytal				
Case	Patient's Age, Yr.	Weight, Kg.	Maximal Single Dose*	Maximal Daily Dose	Average Daily Dose	Number of Days Given	Total Dose	Maximal Single Dose	Maximal Daily Dose	Average Daily Dose	Number of Days Given	Total Dose
1†	4	15.9	108	300	188.6	12	2,264	12.0	29.8	15.1	10	151.0
2	11	24.5	50	220	94.5	11	1,040	....	....	....	..	.....
3	3	15.9	50	270	208.7	16	3,337	....	....	....	..	.....
6	13	34.1	50	280	141.0	20	2,821	....	....	....	..	.....
10	9	31.8	50	209	129.3	23	2,974	....	....	....	..	.....
11†	11	36.4	54	338	170.4	20	3,408	5.2	47.4	32.9	15	494.5
12	9	26.6	68	175	151.0	2	302	7.2	43.3	32.5	8	259.8
13	4	15.5	...	...	.....	..	.....	12.3	49.5	36.3	5	181.7
14	14	31.8	100	146	73.3	3	220	6.0	16.0	12.1	5	60.4
15	13	37.3	35	316	206.5	8	1,652	10.2	25.7	11.3	5	56.6
19	7	25.0	100	300	186.0	7	1,302	7.7	46.0	19.0	8	151.0
20	6	22.7	30	1,000	530.3	8	4,243	8.4	33.8	21.6	6	126.6
25†	15	34.5	49	638	367.0	2	734	9.2	32.4	32.4	1	32.4
26	13	33.2	47	642	642.0	1	642	...	....	....	..	....
27	9	27.3	65	568	308.3	3	925	...	....	....	..	....
28	9	27.3	15	187	155.5	4	622	...	....	....	..	....
29†	14	40.0	18	245	212.0	1.5	319	4.8	40.0	40.0	1.5	60.0
30	9	27.3	25	440	289.2	5	1,446	...	....	....	..	....
31	4	18.1	55	521	470.3	3	1,411	...	....	....	..	....

* All doses expressed in terms of milligrams per kilogram of body weight.

† Patients thus designated received both drugs on corresponding days during the major part of the illness. All others were given only one of the sedatives (at times with a relatively small amount of the other) during any given twenty-four hour period.

The patients above the dark horizontal line recovered, and those below died.

7. (*a*) Ravdin, I. S.; Drabkin, D. L., and Bothe, A. E.: The Effect of Repeated Injections of Sodium Iso-Amyl-Ethyl Barbiturate on Various Viscera, J. Lab. & Clin. Med. **16**:561-566 (March) 1931. (*b*) Bourne, W.; Brueger, M., and Dreyer, N. B.: The Effects of Amytal and Avertin Separately on the Blood: Its Reaction, the Carbon Dioxid Combining Power, and the Concentration; on Body Temperature; on the Function of the Liver; and on the Rate of Secretion and Composition of the Urine, Anesth. & Analg. **10**:85-87 (March-April) 1931. (*c*) Bohn, R. W.: Sodium Amytal Narcosis as a Therapeutic Aid in Psychiatry, Psychiatric Quart. **6**:301-309, 1932. (*d*) Swanson and others.[3f] Schlaepfer and Peters.[6b]

8. Weiss, S.: The Indications and Dangers of Sedatives and Hypnotics with Special Reference to the Barbituric Acid Derivatives, Internat. Clin. **1**:38-66 (March) 1936. Swanson and others.[3f] Schlaepfer and Peters.[6b] Ravdin and others.[7a]

providing 100 mg. of tribromethanol per kilogram of body weight. For such accidents one may employ one or all of the following measures: artificial respiration, external heat, elevation of the foot of the bed, inhalations of a mixture of 5 to 10 per cent carbon dioxide and 95 to 90 per cent oxygen respectively and intramuscular injections of coramine (a 25 per cent solution of pyridine betacarbonate in diethylamine) in 1 cc. doses (or ephedrine sulfate on the basis of 1 mg. per kilogram) until respiratory depression is overcome and the blood pressure has approached a normal level.

As 5 of the patients in the fatal cases recorded in table 2 had received unusually intensive treatment by administration of avertin with amylene hydrate, the suggestion may be offered that overenthusiastic sedative therapy may at times reduce the chances of recovery. Despite the fact that the patient in case 20 recovered with a very high dosage, a more conservative employment of sedatives is to be recommended for routine use. Nevertheless, inadequate sedation should be avoided because of the fact that uncontrolled convulsions may precipitate a fatal outcome.

SERUM THERAPY

A study of the literature reveals that considerable confusion prevails concerning the therapeutic value of specific antitoxin for patients with tetanus. The evidence may be interpreted as either against [9] or in favor of [10] specific serotherapy. Although table 3 suggests that the use of tetanus antitoxin may play a distinct role in reducing the mortality rate, from a clinical standpoint it is exceedingly difficult to differentiate between those individual patients who will and those who will not

9. Huntington, R. W., Jr.; Thompson, W. R.. and Gordon, H. H.: The Treatment of Tetanus with Antitoxin: An Analysis of the Outcome in Six Hundred and Forty-Two Cases, Ann. Surg. **105**:93-96 (Jan.) 1937.

10. (*a*) Abel, J. J., and Chalian, W.: Researches on Tetanus: VIII. At What Point in the Course of Tetanus Does Antitetanic Serum Fail to Save Life? Bull. Johns Hopkins Hosp. **62**:610-633 (June) 1938. (*b*) Abel, J. J.; Hampil, B.; Jonas, A. F., Jr., and Chalian, W.: Researches on Tetanus: VII. Time Required for Fixation of Fatal Quantity of Tetanus Toxin, ibid. **62**:522-563 (May) 1938. (*c*) Florey, H., and Fildes, P.: Treatment of Tetanus in Rabbits with Large Intrathecal Doses of Antitoxin, Brit. J. Exper. Path. **8**:393-397 (Oct.) 1927. (*d*) Donitz, W.: Ueber das Antitoxin des Tetanus, Deutsche med. Wchnschr. **23**:428-430, 1892. (*e*) Kitasato, S.: Heilversuche an tetanuskranken Thieren, Ztschr. f. Hyg. u. Infektionskr. **12**:256-260, 1892. (*f*) Madsen, T.: Ueber Tetanolysin, ibid. **32**:214-238, 1899; Ueber Heilversuche in Reagensglas, ibid. **32**:239-245, 1899. (*g*) Spaeth, R.: Serum Therapy of Tetanus: A Test for Estimating Adequate Dosage of Antitoxin, to be published. (*h*) Moschcowitz, A. V.: Tetanus: A Study of the Nature, Excitant, Lesions, Symptomatology, and Treatment of the Disease, with a Critical Summary of the Results of Serum Therapy, Ann. Surg. **32**:219-250, 416-445 and 575-601, 1900.

respond favorably to antitoxin therapy. Recovery may occur in the presence of apparently ominous signs and symptoms.[10a] On the other hand, a persistent focus of infection may continue to discharge toxin, which if not neutralized by specific antibodies may lead to a fatal outcome for a patient who presents only mild evidences of tetanus at the time of hospitalization.[10a] For these reasons, I concur in the teaching [10a] that early and intensive serum treatment should be given to all patients with tetanus in order to save, perhaps, only a limited number.

As to the routes of election for the administration of antitoxin, one group favors the intrathecal channel [11] and another the intravenous or the intramuscular, or both, to the exclusion of the intraspinal approach,[12]

TABLE 3.—*Relation Between Serum Therapy and Mortality in Cases of Tetanus*

	Incubation Periods of 10 Days or Less			Incubation Periods Over 10 Days			Total		
Serum Therapy	Cases	Deaths	Per Cent Mortality	Cases	Deaths	Per Cent Mortality	Cases	Deaths	Per Cent Mortality
Not given.....	331	315	95.1	239	147	61.5	570	462	81.0
Given.....	1,142	807	70.6	775	281	36.2	1,917	1,088	56.7

The following numbers of cases were selected from the sources given. No serum therapy: Cook County Hospital,[35] 10; Permin,[14a] 244; Richter, cited by Moschcowitz,[10h] 205; Poland, cited by Moschcowitz,[10h] 111. Serum therapy: Moschcowitz,[10h] 236; Graves,[12a] 695; Miller and Rogers,[12b] 30; Vener, Bower and McKillop,[17a] 99; Cook County Hospital,[35] 134; Graffagnino and Davison,[44e] 416; Permin,[14a] 307.

11. Ashhurst, A. P. C.: The Prognosis of Tetanus, J. A. M. A. **87**:2089-2090 (Dec. 18) 1926. Andrewes, F. W.: On the Intrathecal Route for Administration of Tetanus Antitoxin, Lancet **1**:682-686 (May 5) 1917. Park, W. H., and Nicoll, M.: Experiments on Curative Value of Intraspinal Administration of Tetanus Antitoxin, J. A. M. A. **63**:235-238 (July 18) 1914. Sherrington, C. S.: Observations with Antitetanic Serum in the Monkey, Lancet **2**:964-966 (Dec. 29) 1917. Vener, H. I.: Tetanus: Treatment, California & West. Med. **48**:193-196 (March) 1938.

12. (*a*) Graves, A. M.: Tetanus in New Orleans, Ann. Surg. **92**:1075-1086 (Nov.) 1930. (*b*) Miller, R. H., and Rogers, H.: Present State of Tetanus, with Special Regard to Treatment, J. A. M. A. **104**:186-191 (Jan. 19) 1935. (*c*) Dean, H. R.: Report on Twenty-Five Cases of Tetanus to the Medical Research Committee, Lancet **1**:673-680 (May 5) 1917. (*d*) Freedlander, S. O.: Treatment of Tetanus, Am. J. M. Sc. **161**:819-823 (June) 1921. (*e*) Klemmer, P. A., and Crossland, E. S.: The Treatment of Tetanus in the Hospitals of Lancaster, Pa., over a Period of Thirty Years, ibid. **187**:700-705 (May) 1934. (*f*) Paterson, A. E.: Tetanus: Its Diagnosis and Treatment, with a Summary of Twenty-Six Consecutive Cases, M. J. Australia **1**:832-834 (June 28) 1930. (*g*) Silverthorne, N., and Hart, A. P.: Antitoxin in Large Doses in Tetanus, Canad. Pub. Health J. **22**:181-184 (April) 1931. (*h*) Taylor, F. W.: Study of the Treatment in Acute Tetanus, J. A. M. A. **102**:895-898 (March 24) 1934. (*i*) Boyce and McFetridge.[2c] Cole.[2g] Huntington.[2p] Jeans.[2q] Spaeth.[2b]

while a third adopts either a neutral or a wavering point of view.[13] Although the traditional teaching has been that tetanus toxin reaches the central nervous system by way of the peripheral nerve trunks,[14] more recent evidence indicates that the sole avenue of spread is the blood stream.[15] It would appear logical, therefore, to administer serum exclusively by the intravenous or the intramuscular route. Furthermore, intraspinal and intracisternal therapy are to be avoided because of the excitement caused the patients, the technical difficulties encountered in employment of such procedures in the presence of highly spastic states and the danger of inducing sterile or septic meningitis [1] in subjects already dangerously hyperexcitable. My experiences confirm those of Dietrich,[1] who observed "acutely fatal" outcomes directly attributable to intrathecal serotherapy. Since rapid absorption of antitoxin is desirable, either the intravenous or the intramuscular channel should be employed whenever feasible. The latter route is probably satisfactory for those patients with mild evidences of tetanus first admitted to the hospital for treatment after the fourth day of the disease, whereas the intravenous

13. Leishman, W. B., and Smallman, A. B.: Recent Cases of Tetanus in the British Expeditionary Force, Lancet **1**:131-139 (Jan. 27) 1917. Golla, F.: A Comparison of Subcutaneous with Intravenous and Intrathecal Administration of Tetanus Antitoxin in Experimental Tetanus, ibid. **1**:686 (May 5) 1917. Greenwood, M.: A Statistical Note on an Analysis of Cases of Tetanus in the British Expeditionary Force, ibid. **1**:687-688 (May 5) 1917.

14. (*a*) Permin, C.: Experimentelle und klinische Untersuchungen über die Pathogenese und Therapie des Starrkrampfes, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **27**:1-72, 1914. (*b*) Meyer, H., and Ransom, F.: Untersuchungen über den Tetanus, Arch. f. exper. Path. u. Pharmakol. **49**:369-416, 1903. Marie, A., and Morax, V.: Recherches sur l'absorption de la toxine tétanique, Ann. Inst. Pasteur **16**:818-832, 1902. Robertson, H. E.: The Distribution of Tetanus Toxin in the Body, Am. J. M. Sc. **152**:31-48 (July) 1916. Teale, F. H., and Embleton, D.: The Paths of Spread of Bacterial Exotoxins, with Special Reference to Tetanus Toxin, J. Path. & Bact. **23**:50-68 (Oct.) 1919. Bromeis, H.: Die Wanderungsgeschwindigkeit des Tetanusgiftes in Tierkörper, Deutsche Ztschr. f. Chir. **250**:402-410, 1938.

15. Abel, J. J.; Evans, E. A., Jr.; Hampil, B., and Lee, F. C.: Researches on Tetanus: II. The Toxin of the Bacillus Tetani Is Not Transported to the Central Nervous System by Any Component of the Peripheral Nerve Trunks, Bull. Johns Hopkins Hosp. **56**:84-114 (Feb.) 1935. Abel, J. J.; Hampil, B., and Jonas, A. F., Jr.: Researches on Tetanus: III. Further Experiments to Prove that Tetanus Toxin Is Not Carried in Peripheral Nerves to the Central Nervous System, ibid. **56**:317-336 (June) 1935. Abel, J. J.; Evans, E. A., Jr., and Hampil, B.: Researches on Tetanus: V. Distribution and Fate of Tetanus Toxin in the Body, ibid. **59**:307-391 (Nov.) 1936. Abel, J. J.; Firor, W. M., and Chalian, W.: Researches on Tetanus: IX. Further Evidence to Show that Tetanus Toxin Is Not Carried to Central Neurons by Way of the Axis Cylinders of Motor Nerves, ibid. **63**:373-403 (Dec.) 1938. Abel, J. J.: On Poisons and Disease and Some Experiments with the Toxin of the Bacillus Tetani, Science **79**:121-129 (Feb. 9) 1934. Abel and Chalian.[10a] Abel and others.[10b]

injection would seem, at least theoretically, more desirable for those hospitalized earlier in the disease (see section on prognosis). In the treatment of patients known or suspected to be sensitive to horse serum, antitoxin should be injected by muscle rather than by vein.

The amounts of antitoxin recommended have ranged from doses as low as 20,000 to 30,000 units to levels of 50,000 and above.[17] At times the dose of antitoxin has been limited only by the amounts available. In 1 instance [12g] 2,867,000 units was given in four days by a continuous intravenous drip, and in another [17b] 3,460,000 units by muscle was given over a period of forty-one days. In respect to the number of injections, one school points to the rationale of a single dose, or at most two doses,[18] as in the more modern therapy of diphtheria, while the other favors the use of repeated injections.[19] A critical evaluation of the various reports studied leaves one with the conviction that reliance cannot be placed on conventional statistical methods to determine the optimal dose of tetanus

TABLE 4.—*Relation Between Dose of Antitoxin and Clinical Outcome in 33 Patients Treated by the Newer Routine*

Dose of Antitoxin in Units	Mild		Moderate		Severe		Total		
	Recovery	Death	Recovery	Death	Recovery	Death	Recovery	Death	R/D
80,000-82,000	..	..	..	..	1	1	1	1	1.0
60,000-62,500	1	0	7	1	5	4	13	5	2.6
30,000-40,000	1	0	2	0	1	1	4	1	4.0
10,000-20,000	5	0	1	0	0	1	6	1	6.0
Not stated	..	..	..	..	0	1	0	1	...

R/D: ratio between recoveries and deaths.

antitoxin. For example, table 4 would suggest that the case fatality rate increased as the dose of serum was raised. Obviously, this does not mean that the greater amounts of serum were responsible for the increased number of deaths. Analysis of table 4 reveals that classification of the cases in terms of the relative severity of the disease yields groups too small to justify even attempts at statistical analysis. A number of other variable factors, discussed under the heading of prognosis, further limit such a method of study.

16. Footnote deleted.

17. (*a*) Vener, H. I.; Bower, A. G., and McKillop, J. E.: Clinical Tetanus: A Study of One Hundred and Thirty-One Cases, California & West. Med. **39**: 309-312 (Nov.); 374-380 (Dec.) 1933. (*b*) Cables, H. A.: The Amount of Antitoxin Used in a Case of Tetanus, J. A. M. A. **110**:1271-1272 (April 16) 1938. (*c*) Boyce and McFetridge.[2c] Jeans.[2q] Spaeth.[2b'] Wiedkopf.[2e'] Graves.[12a] Freedlander.[12d]

18. Cole.[2g] Jeans.[2q] Spaeth.[2b']

19. Wiedkopf.[2e'] Graves.[12a] Miller and Rogers.[12b] Freedlander.[12d] Paterson.[12f] Silverthorne and Hart.[12g]

Since the available evidence would indicate that tetanus is a blood-borne disease, the aim of serotherapy logically should be the maintenance of a liberal excess [20] of antitoxin in the blood stream until convalescence is definitely established. According to my experience, a high titer of antitoxin would seem necessary during the first two weeks of the disease and a much lower one up to the time of discharge from the hospital. The vast majority (81 per cent) of my patients could be released after a stay in the hospital of three weeks or less, and the maximum period of hospitalization for any single patient was thirty-seven days.

Unfortunately, neither the clinical outcome nor the appearance of the patient gives any clue to the level of antitoxin present in the circulating blood.[21] For this reason, actual titrations have been necessary. Dean [12e] found that as late as thirty-nine days after a single intravenous injection of 30,000 units of tetanus antitoxin the blood of the patient may contain appreciable amounts. Titration studies conducted by me [10g] have demonstrated that one intravenous dose of 60,000 units is followed by a significant antitoxic titer which may persist at progressively lower levels for as long as six weeks. Cole and Spooner [22] observed that after one intravenous injection of 200,000 units the blood of 3 patients contained from 1.25 to 3.33 units of antitoxin per cubic centimeter twenty-eight to thirty-two days later. In another patient, 0.1 unit per cubic centimeter was detected sixty-three days after the aforementioned dose of serum. These studies suggest that single intravenous or intramuscular doses of 30,000 to 60,000 units or more should be adequate. The accom-

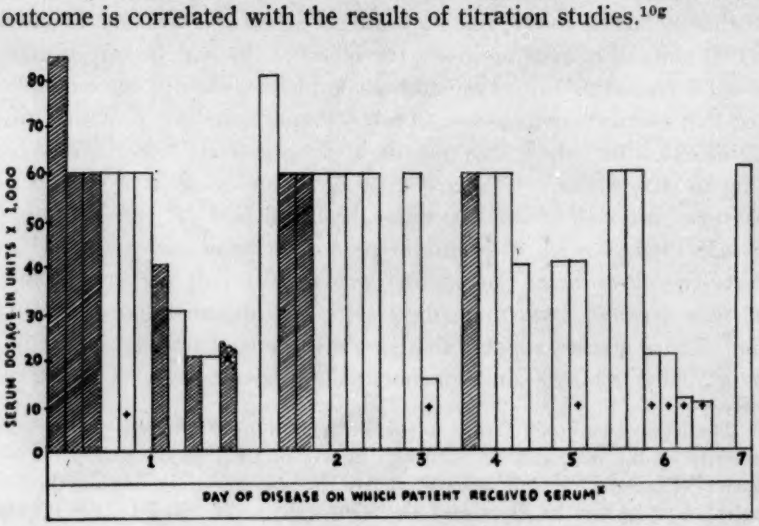
20. The level of antitoxin needed to prevent tetanus must of necessity vary with the severity of the intoxication. Although figures of 0.001 to 0.1 unit per cubic centimeter (Cooke, J. V.: Combined Active Immunization for Diphtheria and Tetanus: A Plea for Its Routine Use, South. M. J. **31**:158-161 [Feb.] 1938. Boyd, J. S. K.: Active Immunization Against Tetanus, J. Roy. Army M. Corps **70**:289-307 [May] 1938. McBryde, A.: Tetanus Immunization with Alum Precipitated Toxoid, South. M. J. **30**:565-567 [June] 1937. Cowles, P. B.: Tetanus Immunization, Yale J. Biol. & Med. **9**:409-416 [May] 1937. Sneath, P. A. T., and Kerslake, E. J.: Persistence of Tetanus Antitoxin in Man Following the Administration of Active Immunization, Brit. M. J. **2**:290-291 [Aug. 17] 1935; Active Immunization Against Tetanus, Internat. M. Digest **32**:183-188 [March] 1938. Otten, J., and Henneman, I. P.: Combined [Simultaneous] Immunization Against Tetanus, J. Path. & Bact. **49**:213-227 [July] 1939) have been stated to be the clinically protective levels, Sneath and Kerslake have suggested the desirability of accepting the latter value until a more definite standard has been established. It is to be remembered that the unit of tetanus antitoxin possesses ten times the potency of antidiphtheritic serum, the former neutralizing 1,000, and the latter 100, minimum lethal doses of specific toxin [Cooke]).

21. Spaeth.[10g] Dean.[12e]

22. Cole, L., and Spooner, E. T. C.: The Treatment of Tetanus, with Observations on the Fate of Injected Antitoxin, Quart. J. Med. **4**:295-319 (July) 1935.

panying chart suggests that mildly to moderately ill patients seeking treatment near the end of the first week of the disease may recover with doses of 40,000 units or less.

On the basis of the aforementioned studies, I propose a routine dose of 60,000 units for patients admitted for serotherapy during the first five days of the disease and a dose of 40,000 units for the mildly to moderately ill patients first treated later. Larger amounts cannot be criticized except to the extent that they may increase discomfort to the patient, the cost of treatment and the likelihood of both immediate and delayed serum reactions. It cannot be denied that doses smaller than those advocated by this clinic might be equally effective. The settlement of this problem must await further investigations in which the clinical outcome is correlated with the results of titration studies.[10g]



Relation between the dose of antitoxin and the clinical outcome in the 33 patients of the new series. The asterisk indicates that the dosage was not recorded. The point marked *X* indicates the day on which the patient was admitted to the hospital. The plus sign indicates mild tetanus. In all other cases the condition was moderate or severe. The shaded columns represent deaths.

Although the dosage of tetanus antitoxin is frequently calculated on the basis of body weight, in this clinic and in cases of given severity the amounts of serum are the same regardless of the weight of the patient. If antitoxin is administered on the basis of body weight, the child will get much less than the adult. Behring and Knorr [23] demonstrated that, other conditions being equal, the amount of serum needed to prevent fatal

23. Behring, E., and Knorr, J.: Ueber den Immunisierungswerth und Heilwerth des Tetanusheilserums bei weissen Mäusen, Ztschr. f. Hyg. u. Infektionskr. **13**: 407-426, 1893.

tetanus in experimental animals increases out of proportion to the variable increments of toxin employed. This observation, applied to tetanus in human beings, would indicate that the requirements of serum per unit of body weight should be greater for children than for adults. From the clinical standpoint, to meet the variable requirements imposed by differences in body weight, it would appear satisfactory to disregard the body weight in determining the amounts of serum to be given.

Reactions caused by sensitivity to horse serum not infrequently cause considerable alarm. During the intravenous injection of 10,000 units of tetanus antitoxin, the patient in case 9 (table 1) showed a severe immediate reaction, with a temperature of 106 F., chills and generalized urticaria. The records indicate that of 33 patients in the old series, 6 had acute thermal reactions to serum. In no instance did death follow these accidents. Delayed serum sickness occurred on the fourth to the twelfth day after injection of antitoxin in 17 of 26 patients of the new series who either recovered or lived long enough to show late reactions to foreign protein.

In addition to proper preparation and administration of tetanus antitoxin,[24] employment of the more refined serums is desirable to reduce the incidence of the aforementioned reactions. The serum of actively immunized human donors,[1] preferably highly concentrated or in lyophile form, would be highly desirable. However, to prevent acute accidents from the serums at present available, it is necessary to detect the patients who are sensitive to horse serum and to observe certain precautions in the administration of antitoxin. To identify the sensitive patients, I rely mainly on the history and physical examination to determine whether the patient or his relatives have shown evidences of allergy and to ascertain whether the patient has received injections of material containing horse serum. This includes diphtheria toxin-antitoxin. For various reasons, I have not uniformly employed the conventional sen-

24. Tetanus antitoxin must be properly heated, by immersing it for about thirty minutes in water kept at approximately 100 F. The intramuscular injection of cold serum may cause pain, slow absorption and possibly abscess formation (Hoyne, A. L.: The Pharmacopeia and the Physician: Immunologic Methods in Pediatrics, J. A. M. A. **112**:1581-1584 [April 22] 1939). The intravenous administration of either cold or overheated antitoxin may precipitate a picture resembling shock (Hoyne). To facilitate injection of the serum by the intramuscular route, in the event of a severe reaction following intravenous administration, it is desirable constantly to refill an arsphenamine flask or a container of similar design, with a solution containing 5 cc. of antitoxin to 100 cc. of 5 per cent dextrose solution or physiologic solution of sodium chloride. In this way, unwieldy dilutions for intramuscular injection are avoided.

sitivity tests. Because of the excitement caused by their performance, they had best be omitted if the patient shows any tendency toward convulsions. Furthermore, in the individual case there is no strict correlation between the results of these tests and subsequent reactions after the injection of serum. However, if such tests are to be used, the ophthalmic is preferable to the cutaneous, for, although less sensitive than the cutaneous test, it is stated to be more reliable in predicting acute anaphylactic reactions.[25] It is of interest that Hoyne has not observed a single fatal anaphylactic accident among approximately 20,000 patients with diphtheria given specific serum by vein or by muscle without preliminary tests for sensitivity.

A special problem is encountered when antitoxin must be administered to a patient known to be sensitive to horse serum. Although the use of bovine antitoxin has been recommended on such occasions, its limited immediate availability and the possibility of sensitivity to this material (despite negative cutaneous or ophthalmic reactions) make it an unsatisfactory substitute for general use. As has already been stated, the intravenous injection of horse serum must be avoided. Consequently, the intramuscular route must be employed. In the presence of convulsions, especially those accompanied by cyanosis, fatal asphyxial spasms may be precipitated by the irritation caused by gradual administration of antitoxin in accordance with conventional hyposensitizing methods. Consequently, for such patients I recommend injection of the entire dose at one time, one-half being given deep in each gluteal region. However, for patients free from convulsions the gradual administration[26] of serum is permissible. Whichever method is to be employed, the first injection should be given not earlier than thirty minutes after hypodermic injection of a solution of epinephrine hydrochloride and atropine sulfate in accordance with the following dosage schedule:

	Patient Aged 6 Months	Patient Aged 2 Years	Patient Aged 5 Years	Adult Patient
Epinephrine hydrochloride (1:1,000).....	3 minims (0.18 cc.)	4 minims (0.25 cc.)	5 minims (0.31 cc.)	8 minims (0.49 cc.)
Atropine sulfate.....	1/500 grain (0.12 mg.)	1/250 grain (0.24 mg.)	1/200 grain (0.3 mg.)	1/100 grain (0.6 mg.)

25. Stimson, P. M.: A Manual of the Common Contagious Diseases, ed. 3, Philadelphia, Lea & Febiger, 1940, p. 39.

26. The following method is convenient: 1. Thirty minutes after the injection of atropine sulfate and epinephrine hydrochloride, give 0.1 cc. of a 1:100 dilution of antitoxin subcutaneously. 2. Subsequent doses are given at fifteen minute intervals. The second to fifth injections are 0.1, 0.2, 0.4 and 0.8 cc. of a 1:10 dilution subcutaneously. The remaining injections consist of progressively doubled doses of undiluted serum by the intramuscular route, beginning with 0.1 cc. 3. At hourly intervals, or more often if necessary, during the aforementioned injections, 3 to 5 minims (0.18 to 0.31 cc.) of epinephrine hydrochloride (1:1,000) should be administered hypodermically.

I now employ the aforementioned injections for all serum-treated patients, regardless of known or suspected sensitivity to horse serum. In the event of an acute serum reaction, injections of epinephrine hydrochloride (1:1,000), possibly supplemented with atropine sulfate for the more resistant patients, may be given hypodermically or by vein at appropriate intervals; the foot of the bed may be elevated; body warmth may be maintained by the use of blankets and other safe sources of external heat, and cyanosis and apnea may be controlled with artificial respiration, oxygen inhalations and respiratory stimulants.

In case 1 (table 1) the discomfort associated with delayed serum sickness incited recurrent asphyxial spasms eleven days after hospitalization. Similar experiences have been encountered elsewhere.[27] These observations indicate the importance of effective treatment of delayed serum sickness by topical application of antipruritic agents, supplemented by the oral administration of ephedrine compounds (ephedrine-amytal capsules are commercially available) and parenteral injection of epinephrine hydrochloride (1:1,000) as indicated.

SURGICAL THERAPY

Surgical treatment of tetanus ordinarily is not an emergency procedure. I disagree with Taylor,[12h] who has stated that all patients with tetanus should be admitted to the hospital by way of the operating room. Under all circumstances, operative procedures should be employed only after the patient has been given the benefit of adequate sedative and antitoxin therapy. To submit a patient to the excitement of surgical maneuvers before sleep and relaxation have been induced is to invite potentially fatal acute asphyxial spasms.

The principles of surgery to be followed in the treatment of tetanus are identical with those recommended in the absence of this disease. The physician must evaluate the indications and the type of surgical treatment in terms of the special requirements of each individual case. Under no circumstances should one resort to amputation, excision of local lesions or drainage of purulent collections for the sole purpose of removing the foci at which toxin is being elaborated. Abel and Hampil [28] have pointed out that no evidence is available to indicate that such procedures influence the course of the disease in either human beings or animals with fully developed signs of tetanus. Even under the most favorable circumstances, removal of foci of infection must be performed within an hour or so after injection of a lethal dose of toxin if the life of an experi-

27. Spaeth, R.: Unpublished data.

28. Abel, J. J., and Hampil, B.: Researches on Tetanus: IV. Some Historical Notes on Tetanus and Commentaries Thereon, Bull. Johns Hopkins Hosp. **58**: 343-376 (Dec.) 1935.

mental animal is to be saved.[28] In similar fashion, McClintock and Hutchings,[29] on the basis of critical animal experiments, concluded that amputation of affected members at the very first appearance of active symptoms of tetanus in no way altered the progress of the disease. The animals so treated died in the same time and with the same symptoms as those given no surgical care.

After administration of appropriate quantities of specific serum one may rely on circulating antitoxin to neutralize any toxin which may continue to be discharged from the point of infection. Should tetanus bacilli persist in virulent form after this passive protection has been lost, the possibility of recurrences cannot be denied. For this reason, after alarming signs and symptoms have been successfully controlled, a gentle but careful search for foreign bodies would appear to be a desirable procedure. Even though wounds have healed, splinters or other objects may be discovered by careful surgical exploration (cases 10 and 30, table 1). A history of removal of foreign bodies prior to hospitalization must not be accepted as final, for residual pieces may remain in the focus of infection (cases 6 and 10). If nail puncture wounds appear to be healed, surgical exploration does not seem justifiable (cases 3, 7, 14, 31, 32 and 33). In the presence of purulent collections, débridement, drainage and removal of any foreign bodies from all wounds are indicated. Irrigation with hydrogen peroxide dilute solution of sodium hypochlorite (Dakin's solution), potassium permanganate or some other oxidizing solution may assist in facilitating free drainage and healing. However, such procedures probably do not influence the course of the tetanus intoxication.[30] Although amputations and other disfiguring operations are to be avoided as far as is feasible, if a structure is already hopelessly destroyed surgical removal would seem to be a justifiable procedure (case 21). In the presence of gas gangrene, wide excision of involved areas and the use of sulfanilamide [31] are indicated.

GENERAL MANAGEMENT

The value of treatment by a specially trained group of physicians and nurses has been reflected in the experiences of both myself and others.[17a] A definite reduction in the fatality rate could be obtained if medical centers were to create centralized tetanus wards under the

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29. McClintock, C. T., and Hutchings, W. H.: The Treatment of Tetanus, J. Infect. Dis. **13**:309-320 (Sept.) 1913.

30. Coleman, G. E.: Experimental Study of Tetanus, J. Infect. Dis. **47**:410-415 (Nov.) 1930.

31. Bohlman, H. R.: Gas Gangrene Treated with Sulfanilamide, J. A. M. A. **109**:254-256 (July 24) 1937. Kennedy, W. C.: Therapy of Gas Gangrene with Report of a Case, Illinois M. J. **73**:260-261 (March) 1938.

charge of persons drilled periodically in respect to the details of management. As has already been indicated, printed outlines are desirable to systematize treatment. In this clinic a liberal supply of such forms is kept on hand for the guidance of the hospital staff.

Patients with tetanus should be under constant observation with the benefit of special nursing care for at least forty-eight hours after receiving antitoxin. Such an arrangement is essential because of the not infrequent transition from a mild to a more severe form of the disease during this period. Generalized rigidity, with or without convulsions, is an indication for continued special nursing attention. In the absence of such care patients may succumb to hypostatic pneumonia, dehydration, starvation, physical injuries or sudden fatal asphyxia.

TABLE 5.—*Analysis of Seventeen Cases of Tetanus Complicated with Pneumonia*

	Old Series	New Series	Total
Number of patients with tetanus	33	33	66
Number of patients with pneumonia *	5 (15%)	12 (36.3%)	17 (25.7%)
Deaths among patients with pneumonia	5 (100%)	9 (75%)	14 (82.3%)
Number of necropsies	4	5	9
Necropsy observations in the lungs:			
Bronchopneumonia	3	5	8
Lobar pneumonia	1	0	1
Pneumococcus recovered	0	2 †	2
Time pneumonia first observed:			
Day of disease	2-4	1-5	1-5
Day of hospitalization	1-4	1-4	1-4
Age of patients in years	7-60	3-57	3-60
Severity of tetanus:			
Mild	2	0	2
Moderate	0	2	2
Severe	3	10	13

* Roentgen examination during life revealed consolidation of the upper lobe of the right lung in 1 fatal case of the old series and cloudiness of the base of the left lung in 1 recovered patient of the new series.

† Obtained from the sputum (patient 29) and from the lungs at necropsy (patient 33).

Special attendants may be released when convalescence has reached a stage at which the patient is able to walk or move around the sickroom in an invalid chair. No patient who has had convulsions should be placed under general ward care until the danger of a delayed serum reaction, with a possible recurrence of convulsions, has passed. Such reactions rarely occur later than twelve days after serum treatment. Obviously, in the event of recurrent spasticity or convulsions the physician must exclude malingering by recourse to the use of placebos.

The fact that pneumonia occurred in approximately one fourth of 66 patients (table 5) indicates that both the prevention and the treatment of this complication are of the utmost importance. Procedures adapted to this purpose are as important as serum and sedative therapy. Obviously, prophylaxis must be directed toward the predisposing causes of this complication. Proionged rigidity of the thorax with associated impairment of pulmonary ventilation may be combated with adequate

sedation supplemented with inhalations of 5 to 10 per cent carbon dioxide in oxygen. The inhalations are conveniently given for periods of ten to fifteen minutes at four hour intervals (or oftener if not too disturbing to the patient), but should be withheld if undue excitement is occasioned. A dorsal position should be avoided as far as is feasible by placing the patient on his abdomen or side as much as possible. Frequent tepid sponge baths, protection from drafts and moderate bedclothing reduce the danger of the pneumonia which might otherwise follow excessive perspiration and chilling of the general body surface. To relieve the respiratory difficulty occasioned by collections of saliva or other secretions in the nasopharynx, ordinarily it is sufficient to wipe the patient's lips after he has been induced to blow out this material with the head or the whole body turned to one side. At times mechanical suction, with minimal disturbance to the patient, is necessary. Elevation of the foot of the bed may possibly aid in directing secretions away from the lower part of the respiratory tract. I have found atropine sulfate of little value in preventing pulmonary complications. In fact, the secretions become thick and difficult to expectorate if this drug is employed.

Unfortunately, pneumonia may develop despite employment of the measures suggested. Although table 5 is self explanatory, certain facts are worthy of comment. Fifteen of the 17 patients with pulmonary involvement had moderate to severe forms of tetanus. For this reason, it is of particular interest that pneumonia occurred in 2 patients with mild evidences of tetanus, neither of whom was treated in accordance with the new routine. Both patients were men, the one 60 and the other 21 years of age. Bilateral bronchopneumonia was present in the former and right upper lobar pneumonia in the latter. In both cases the diagnoses were confirmed at necropsy. It is noteworthy that the incidence of pneumonia was significantly greater in the new than in the old series. However, the explanation of this difference must remain a matter of conjecture. The recovery of pneumococci from 2 patients indicates the need of further studies to determine the incidence of this organism or of other bacteria susceptible to specific chemotherapy in the pneumonia which occurs as a complication of tetanus. As may be noted in table 5, the time of onset varied from the first to the fifth day of the disease. In all instances, elevations of temperature of variable degree announced the onset of pulmonary complications. Increased respiratory rates appeared either simultaneously with the onset of fever or a short time after it. Because of the infrequency of examinations of the chest imposed by my principles of treatment, I did not determine the exact intervals required for the appearance of typical pulmonary findings. However, since pneumonia is present in the vast majority of patients with early elevations of temperature not otherwise explainable (see section on prognosis),

failure to detect the characteristic physical findings should not deter one from making a provisional diagnosis of this complication or from instituting early treatment. Nevertheless, although fever and accelerated respirations should suggest a diagnosis of pneumonia, atelectasis and/or acidosis must be excluded by appropriate procedures.

Pneumonia in a patient with tetanus offers a grave, but not a hopeless, prognosis. The occurrence of 3 recoveries among 12 patients with this complication (table 5) justifies the prompt and systematic institution of measures considered to be of value for the pneumonia which occurs in the absence of tetanus. Oxygen therapy should be started early and before respiratory distress becomes pronounced. Homologous serum should be administered intravenously if type-specific pneumococci can be recovered from the sputum, the blood culture or the upper part of the respiratory tract. However, special precautions must be observed to avoid acute anaphylactic reactions because of the fact that the patient has already received antitoxin containing horse serum. Whether or not pneumococci are recovered, the patient should be given a therapeutic trial of sulfapyridine by mouth or of the sodium salt parenterally.[32] Repeated transfusions of citrated blood from suitable donors may be used to combat the associated inanition and anemia and possibly to assist in building up the immunologic defense mechanism.

One should attempt to maintain an optimal fluid and caloric intake with minimal disturbance to the patient. It is to be emphasized that it is much more important to keep the patient quiet than to meet theoretic metabolic needs. A diet high in carbohydrate is desirable. Attempts at feeding by any route should be abandoned immediately should they incite asphyxial convulsions. If sedatives relieve trismus and/or pharyngeal spasm, a liquid or a very soft diet may be given orally. Food is to be offered at the onset of relaxation, and patients are never to be awakened for feedings. Liquids should be fed literally drop by drop by means of medicine droppers with attached rubber tubing. Some patients fare better with glass suction tubes, whereas others drink more easily with the ordinary infant's nursing bottle and nipple. In the presence of intractable difficulty in swallowing one may employ daily intravenous injections of 1,000 to 2,000 cc. of 5 per cent dextrose in Hartmann's buffered solution (sodium lactate in Ringer's solution,

32. Marshall, E. K., Jr., and Long, P. H.: The Intravenous Use of Sodium Sulfapyridine, J. A. M. A. **112**:1671-1675 (April 29) 1939. Taplin, G. V.; Jacox, R. F., and Howland, J. W.: The Use of Sodium Sulfapyridine by Hypodermoclysis, ibid. **114**:1733-1734 (May 4) 1940. I have observed elsewhere the successful use of intravenous injections of sodium sulfapyridine in the treatment of a patient with tetanus acutely ill from complicating pneumonia. The case will be discussed in a future communication.

available commercially). If necessary, veins should be exposed at the ankle or cubital fossa with the region under local anesthesia. Except for the occasional convalescent patient with a markedly swollen tongue, nasal feedings should be avoided because of the danger of inciting asphyxial spasms. Transition to the regular diet should be gradual.

Constipation or retention of urine may be caused by hypertonicity of the sphincters and may occasion abdominal discomfort, at times colicky and difficult of differentiation from the pain incited by tetanic spasms of the abdominal wall. If it is of gastrointestinal origin, relief may be obtained from cleansing enemas and from atropine sulfate given by mouth or by hypodermic injection. To avoid such difficulties, enemas may be required every other day. Two patients of the new series (cases 1 and 23) and 7 of 33 of the old had retention of urine. According to my experiences in this clinic and elsewhere,[27] children require no local measures to relieve distention of the urinary bladder. However, for adults catheterization may be necessary. The patient in case 1 of the new series and 4 of 33 patients of the old required such treatment.

PROGNOSIS

Critical appraisal of the new method of treatment described here requires a comparison of the old and the new series in terms of those features considered to be of prognostic importance.

As a general rule, the more severe the tetanus the earlier the patient seeks medical care.[9] Likewise, the mortality is higher among the patients with the shorter periods of incubation (table 3). Huntington, Thompson and Gordon[9] have pointed out the necessity of considering simultaneously both the severity of the disease, represented by the day treatment is sought, and the incubation period in formulating a prognosis. Four hundred and thirty-seven case records studied by these writers[9] contained information relating to both the incubation period and the duration of symptoms up to the time of hospitalization. The case fatality rate was approximately 64 per cent. Ninety-eight per cent of the deaths occurred among patients hospitalized during the first four days of the disease (irrespective of incubation periods) and 87 per cent among those admitted during the aforementioned interval and with incubation periods of fourteen days or less. Obviously, these results do not mean that early treatment was responsible for the increased mortality rates. In table 6 the method of analysis adopted by Huntington and his associates[9] has been modified by classification of the patients in terms of the relative severity of the clinical pictures of tetanus and by the insertion of notations concerning both the incidence and the character of complications.

Table 6 reveals four important facts. 1. The incidence of mild tetanus was considerably lower in the new series than in the old. Seven of 33 patients of the former, in contrast with 17 among an equal number of the latter, had mild forms of the disease. 2. With but 1 exception, all deaths were of patients with incubation periods of ten days or less. One fatality occurred in a group of 10 patients of the new series from whose histories the periods of incubation could not be determined accurately. 3. All of the 21 deaths occurred among the 47 patients admitted for treatment and given antitoxin in whole or in part during the first four days of the disease. These results reflect the greater incidence of moderate to severe forms of tetanus among those admitted

TABLE 6.—*Analysis of Outcome in Sixty-Six Cases of Tetanus with Reference to Incubation Periods and Duration of Symptoms Up to Time of Hospitalization*

Incubation Period in Days	First Four Days of Disease						Fifth Day or Later						All Patients					
	Mild		Moderate and Severe		Total		Mild		Moderate and Severe		Total		Mild		Moderate and Severe		Total	
	R	D	R	D	R	D	R	D	R	D	R	D	R	D	R	D	R	D
1 to 10 days																		
Old.....	4	2(2)	1	**10(3)**	5	**12**	1	..	1	..	2	..	5	2	2	10	7	12
New.....	2	..	7(1)*	**8(8)**	9	8	..	..	2	..	2	..	2	..	9	8	11	8
Over 10 days																		
Old.....	3	..	1	..	4	..	4	..	1	..	5	..	7	..	2	..	9	..
New.....	..	..	4(1)†	.	4	..	..	..	..	..	..	..	..	..	4	..	4	..
Unknown																		
Old.....	1	..	1	..	2	..	2	..	1	..	3	..	3	..	2	..	5	..
New.....	..	..	2(1)	1(1)	2	1	5	..	2	..	7	..	5	..	4	1	9	1
Total																		
Old.....	8	2	3	10	11	12	7	..	3	..	10	..	15	2	6	10	21	12
New.....	2	..	13	9	15	9	5	..	4	..	9	..	7	..	17	9	24	9

R, recovery; D, died. The figures in parentheses indicate the number of patients with pneumonia. The figures in bold face type include the patients among whom the majority of the deaths occurred.

* One patient had diabetes mellitus.

† One patient had gas gangrene.

early than among the group hospitalized after the fourth day of the disease. Thirty-five of the 47 patients admitted early, in contrast with 7 of 19 hospitalized later, presented moderate to severe evidences of tetanus. Although essentially the same number of patients in the two series were admitted during the first four days of the disease, the incidence of moderate to severe forms of tetanus among those admitted early was definitely greater in the new series than in the old (22 in the former and 13 in the latter group). In similar fashion, among those admitted during the first four days of the disease the incidence of potentially fatal complications was distinctly greater in the new series than in the old. Thus, 5 of 23 patients in the old series, in contrast with 12 of 24 of the new, had pneumonia at some time during

their stay in the hospital. Likewise, if the two series are compared without considering the time of hospitalization, it is noteworthy that the incidence of pneumonia was definitely higher in the new than in the old series; for 12 of 33 of the former, as compared with 5 of an equal number of the latter group, had pulmonary involvement. As to other complications, recovery occurred in 2 moderately to severely ill patients of the new series despite the presence of gas gangrene in 1 and of diabetes mellitus in the other. 4. Eighteen of the 21 deaths occurred among the 26 patients admitted during the first four days of the disease with moderate or severe forms of tetanus which appeared ten days or less after injury. Hence, a comparison of the results obtained by the old and the new methods of treatment may properly be confined to a consideration of these limited groups. In this class of 26 patients, fatal terminations occurred in 10 of 11 of the old series, in contrast with 8 of 15 of the new. These results, apparently in favor of the new series, are less clearly defined if only total case fatality rates are considered, for death occurred in 12 of 33 patients (36.3 per cent) of the old series and in 9 of an equal number (27.3 per cent) of the new. However, if the 24 "mild cases" are excluded, fatalities occurred in 10 of 16 (62.5 per cent) of the old, in contrast with 9 of 26 (34.6 per cent) of the new series.

In respect to both the severity and the site of the local lesions, the old and the new series were essentially comparable. Although a review of the literature indicates that foci of infection in the uterus (puerperal sepsis, abortions) or in mutilated extremities (infected compound fractures, gangrene from crushing injuries or other causes) may reduce the chances of recovery, none of the deaths among my patients could be attributed directly to the local lesions. As to the distribution of the local injuries, table 7 reveals that approximately 85 per cent of the patients in each group had points of infection in the lower and/or upper extremity, and the proportion of those with lesions at these respective sites was about the same in each group. However, any differences which might have been encountered need not have prevented a satisfactory comparison of the two groups; for the observations of both myself and others [10g] are at variance with the current belief that the closer the local focus to the central nervous system the greater is the death rate. This point of view is not invalidated by the fact that the case fatality rate in the combined series of 66 patients was about 12 per cent lower among the 41 with lesions of the lower extremity than among the 15 with injuries of the upper extremity. These differences are more apparent than real.[10g]

The patient's age must be considered in formulating a prognosis, for the mortality from tetanus seems to be highest in the extremes of

life. It has been pointed out by Cooke [33] that at least 50 per cent of all deaths from this disease occur in children under 15 years of age. Vener and his associates [17a] recorded no recoveries among 7 patients who were older than 50 years. Perusal of table 8 confirms these observations, with the exception that only 2 deaths occurred among 7 patients over 50 years of age. In the old series the case fatality rates were distinctly higher in the youngest and oldest age groups (46.4 and 33.3

TABLE 7.—*Site of Injury in Relation to Mortality*

	Old Series				New Series				All Patients			
Site of Local Lesion	No. of Patients	Percentage of All Patients	No. of Deaths	Percentage Mortality	No. of Patients	Percentage of All Patients	No. of Deaths	Percentage Mortality	No. of Patients	Percentage of All Patients	No. of Deaths	Percentage Mortality
Upper extremity.....	8	24.2	3	37.5	7	21.2	1	14.3	15	22.7	4	26.6
Lower extremity.....	20	60.6	9	45.0	21	63.6	7	33.3	41	62.1	16	39.0
Head and neck region	2	6.1	..	....	..	....	..	....	2	3.0	..	....
Unknown or indeterminate.....	3	9.1	..	....	5	15.2	1	20.0	8	12.1	1	12.5
Total.....	33	100.0	12	36.3	33	100.0	9	27.3	66	99.9	21	31.8

TABLE 8.—*Age in Relation to Mortality*

	Old Series					New Series				
Age Period in Years	No. of Patients	Percentage of All Cases	No. of Deaths	Percentage of All Deaths	Percentage Mortality	No. of Patients	Percentage of All Cases	No. of Deaths	Percentage of All Deaths	Percentage Mortality
1 to 15	13	39.4	6	50.0	46.4	30	91	9	100	30.0
15 to 30	7	21.2	2	16.6	28.6	..	..	..	...	....
30 to 50	7	21.2	2	16.6	28.6	2	6	..	...	....
50 to 70	6	18.2	2	16.6	33.3	1	3	..	...	....
Total	33	100.0	12	99.8	36.3	33	100	9	100	27.3

per cent respectively), and two thirds of all the deaths occurred in these age periods. In the new series, all of the 9 deaths took place among patients whose ages were 15 years or less. Comparison of the old and the new series from the standpoint of apparently unfavorable age incidence indicates that the latter represents a more severe condition. Nineteen of 33 patients in the old series, in contrast with 31 of 33 in the new, were included in the age periods in which the mortality

33. Cooke, J. V.: Combined Active Immunization for Diphtheria and Tetanus: A Plea for Its Routine Use, South. M. J. **31**:158-161 (Feb.) 1938.

ordinarily may be expected to be highest, namely, up to 15 and over 50 years.

The temperature in cases of uncomplicated tetanus is ordinarily normal. As is noted in table 9, 45 patients had fever at some time during their course in the hospital. Twenty-one of these 45 patients died. In contrast, no deaths occurred among the 21 patients who had normal temperatures. This difference in clinical outcome between the febrile and afebrile patients was correlated with the presence of pathologic states—caused by the complications of tetanus, the local lesions or therapeutic measures—in 36 of the 45 with fever, in contrast with the absence of such conditions among those who had normal temperatures. As might be anticipated, the cause of the fever, rather than its level, was of prognostic significance. When the rise in temperature could be attributed to pneumonia, the outlook was particularly grave (tables 5 and 9). Thus, of the 17 patients with pneumonia, 14 died, and

TABLE 9.—*Analysis of Clinical Outcome in Forty-Five Patients with Tetanus and Elevated Temperature*

Cause of Fever	Old Series		New Series		Total	
	R	D	R	D	R	D
Pneumonia	..	5	3	9	3	14
Serum therapy	12 *	..	1 †	..	13	..
Local infection	..	..	1	..	1	..
Pathologic change in central nervous system	..	1 §	..	..	..	1
Otitis media	1	..	1	..	2	..
"Upper respiratory infection"	..	..	1	..	1	..
Tribromethanol reaction	..	..	1	..	1	..
Preterminal rise only	..	1	..	..	..	1
Unknown	..	5	3	..	3	5
Total	13	12	11	9	24	21

* Six patients had acute thermal reactions to antitoxin, with temperature peaks of 104 to 107 F.

† Acute thermal reaction with temperature of 106 F.

§ This patient had received serum intrathecally. Necropsy revealed acute leptomeningitis and deposits of coagulated blood over the left temporal and occipital lobes and small arachnoid hemorrhages over the superior surface of the right lobe of the cerebellum and the lateral surface of the right temporal lobe.

pulmonary involvement was detected in 14 of 21 fatal cases, in contrast with its demonstration in only 3 of 24 recoveries. As may be noted from table 9, with the exception of the patient with gross pathologic change in the central nervous system, fever caused by known conditions other than pneumonia was of benign import. This fact is of particular interest because of the occurrence of 7 recoveries (6 in the old series and 1 in the new) despite acute thermal reactions to antitoxin with temperature peaks of 104 to 107 F. My observations would indicate that the time of onset of fever may be of prognostic importance. Three patients showed elevations in temperature during the second week of hospitalization; all had benign complications (otitis media or other "upper respiratory infection") and recovered. In contrast, all of the

21 deaths occurred among the 42 patients whose fever appeared during the first week of hospitalization. Obviously, the fact that pneumonia explained the fever in 17 of these 42 patients does not imply that pulmonary involvement is always of early onset, for its late appearance has been observed elsewhere.[27] Likewise, it is to be emphasized that the early appearance of fever does not necessarily indicate the presence of pneumonia, for this complication could not be held accountable for the elevations in temperature in 25 of 42 patients.

The total duration of the disease is of prognostic importance. Other conditions being equal, the longer the patient survives, the greater is the chance of recovery. Table 10 indicates that at least 90 per cent of all the fatalities occurred during the first ten days of the disease. However, later deaths may not infrequently occur. Of the 45 delayed deaths reported by Anders and Morgan,[34] 13 occurred after the twentieth day of the disease. Late deaths may be precipitated by complications, particularly pneumonia. This complication was the apparent cause of the 5 deaths which occurred after the tenth day in the Cook County Hospital series.[35] As may be noted from table 10, conditions not related to tetanus may account for late fatalities. Despite the fact that the vast majority of deaths occur during the first ten days of the disease and although late fatalities may be precipitated by conditions not directly related to tetanus, it is advisable to administer specific serum to all patients. For example, in the Cook County Hospital series the use of antitoxin had been delayed beyond the first week of the disease (ninth to eleventh days) in the cases of 3 of the 5 patients who died after the tenth day. Although pneumonia was the apparent cause of death in all of these 5 patients, it is to be restated that pulmonary involvement is more likely to appear in those with the more severe forms of tetanus. For this reason, among others, it would seem advisable to employ antitoxin in an attempt to minimize the degree of advance in the clinical signs of tetanus.

DIAGNOSIS

In the typical case of tetanus the diagnosis is relatively easy if the physician properly evaluates the history of injury, premonitory complaints and physical findings. However, in cases in which there are atypical modes of onset diagnostic difficulties may be encountered.

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34. Anders, J. M., and Morgan, A. C.: Tetanus: A Preliminary Report of a Statistical Study, J. A. M. A. **45**:314-322 (July 29) 1905.

35. Review of Cases of Tetanus Treated at Cook County Hospital, Chicago, from 1920 to July 1933, including those previously reported by Calvin, J. K., and Goldberg, A. H.: The Prognosis of Tetanus, J. A. M. A. **94**:1977-1981 (June 21) 1930. These cases will be discussed in a future communication.

Because of the danger of allowing an advance in the disease if serum is withheld,[10a] it is advisable to administer antitoxin even when the diagnostic data are inconclusive. If convulsions or marked generalized rigidity are present, I favor the omission of spinal puncture even for diagnostic purposes, except when absolutely essential. Fatal asphyxial spasms may be precipitated by spinal punctures.

As is indicated in table 1, frequently the history and the examination reveal either no points of injury or apparently trivial lesions. Five patients volunteered no histories of trauma; 4 showed no local lesions whatsoever, and in 12 of 29 with demonstrable foci apparent healing

TABLE 10.—*Duration of Tetanus at Time of Death*

	Total Duration of Disease *				
	10 Days or Less		Over 10 Days		
Source of Case Reports	No. of Deaths	Percentage of Total Deaths	No. of Deaths	Percentage of Total Deaths	Comment
Iowa University Hospitals					
Old series.....	12	100.0	...	....	Antitoxin used for all patients
New series.....	9	100.0	...	....	Antitoxin used for all patients
Cook County Hospital [35] 1921 to 1933 †	106	95.5	5	4.5	Except in the cases of 9 patients who died early, antitoxin was used therapeutically
Anders and Morgan [34].....	419	90.3	45	9.7	Includes patients treated with and without antitoxin
Vener, Bower, McKillop [17a] *	68 §	97.1	2 §	2.9	Antitoxin employed except for an unstated number who were moribund on admission

* Refers to the time which elapsed from onset of the disease, except in the report of Vener, Bower and McKillop,[17a] which is based on the total hospital residence for tetanus.

† The duration of the disease could be detemined in only 111 of 117 fatal cases.

§ Of the late deaths reported by these writers, only 2 can be properly considered as having occurred after the tenth day of hospitalization for tetanus. The one death took place on about the twentieth day of hospitalization following an acute anaphylactic reaction as a result of the reinjection of antitetanic serum, and the other occurred on the twenty-eighth day in the hospital, from generalized tuberculosis.

was present at the time of hospitalization. In 1 instance (case 30) the local lesion was first detected at the necropsy table. In case 11 a very tiny puncture wound without external signs of inflammation harbored a splinter surrounded by foul-smelling pus. In my experience, detection of the organism is of relatively little value in diagnosis. Bacillus tetani was recovered in only 4 of 33 cases of the new series and in 10 of 33 of the old series.

Premonitory symptoms may be absent or may precede typical physical findings by an interval of one or more days. Their prompt recognition is exceedingly important, because they indicate the need of early and adequate serotherapy. They consist of restlessness, insomnia, irritability, headache and soreness or slight stiffness of the

muscles of the jaw, pharynx, neck, back, abdominal wall or extremities. These complaints represent incipient stages of spasticity which frequently are difficult to demonstrate by physical examination. An awkward, spastic gait is frequently seen early, and its prompt detection assists in establishing a diagnosis before typical trismus appears.

The physical findings in a case of fully developed tetanus are characteristic. They consist of trismus of variable degrees, difficulty in swallowing caused by spasms of either the pharyngeal or the masseter muscles, cervical rigidity (at times associated with opisthotonos), risus sardonicus, generalized and persistent spasticity in the musculature of the trunk, abdominal wall and extremities, awkwardness on locomotion, hyperactivity of the deep tendon reflexes in most instances and urinary suppression and constipation secondary to hypertonicity of the sphincters. Superimposed on this persistent basal rigidity, acute tonic spasms of variable intensity may appear at irregular and unpredictable intervals. If not under the influence of sedative drugs, the victim of tetanus has a clear mind, unclouded by a malady in which dimness of the sensorium would mitigate the degree of suffering. If complications are absent, the temperature is normal. Nevertheless, profuse perspiration may be observed in practically every patient with a well developed form of the disease.

Cases of atypical tetanus are not infrequently encountered.[36] Abel and Hampil [28] have called attention to the marked variety not only in the initial signs and symptoms of tetanus but in their relative order of appearance. Trismus may be absent,[36a] or it may not be the first sign of tetanus;[37] at times it may follow, rather than precede, rigidity of the external abdominal,[12f] pharyngeal [28] and truncal or other skeletal muscles. In some patients the degree of masseter spasm may be less than one would anticipate from the amount of rigidity of the abdominal muscles. Paterson [12f] has pointed out that such a situation not infrequently leads to an erroneous diagnosis of acute abdominal disease. Spasticity of the masseter muscles may disappear or become less evident under the influence of sedatives. The generalized hypotonia present in comatose patients may lead to the disappearance of trismus. Very mild tetanus, particularly if the patient is first seen during convalescence, may present evidences of generalized hypertonicity in the absence of trismus. Rigidity of other muscle groups, especially those of the trunk and abdominal wall, may outlast trismus by days or even by several weeks.

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36. (*a*) Bruce, D.: Tetanus: Analysis of 1,458 Cases Which Occurred in Home Military Hospitals During Years 1914-1918, J. Hyg. **19**:1-32 (July) 1920. (b) Abel and Hampil.[28] Dietrich.[1]

37. Bruce.[36a] Abel and Hampil.[28] Paterson.[12f]

Table 11 shows the time relation of trismus to other signs of tetanus as observed in the 33 patients considered in table 1.

Trismus was either slight or present only intermittently in 4 of the patients who presented this sign at the onset. When trismus appeared after other signs, the interval was approximately one to two days. The diagnosis of generalized tetanus without trismus was confirmed bacteriologically in case 23 but not in case 14.

At times tetanus must be differentiated from acute meningitis (case 16), poliomyelitis (cases 13 and 20), hydrophobia, hysteria, tetany, strychnine or other poisoning, acute abdominal inflammatory conditions, local causes of trismus (retropharyngeal or peritonsillar abscess, inflammations in the teeth or jaws, mumps), meningismus (particularly that sometimes encountered after prophylactic injections of antitetanic serum) and encephalitis. In respect to the last it is important to note that focal neurologic findings, such as are frequently encountered in encephalitis, were observed in case 11 ("left facial palsy") and in 3 patients with tetanus of the old series, 2 of whom had unilateral facial paralysis and 1 a divergent strabismus.

TABLE 11.—*Occurrence of Trismus*

Trismus at onset	25
Trismus after other signs	
Rigidity of external abdominal muscles	2
Rigidity of other trunk muscles	2
Spasm of pharyngeal muscles	2
Generalized tetanus without trismus	2

PROPHYLAXIS

Surgical care of local lesions as a means of preventing tetanus is attended by certain limitations. Analysis of table 1 reveals that tetanus may follow relatively minor injuries and that frequently no local focus can be detected. Theoretically, removal of wide areas of tissues from the sites of local injuries would seem to be desirable. However, for general use such procedures are not feasible, because few patients would be submitted to such extensive surgical treatment of wounds which appear innocent. In certain instances, a number of incisions would be indicated if the aforementioned principle were to be followed (cases 8, 17, 27, 28, 30 and 31). Furthermore, despite timely removal of foreign bodies, the spores of the tetanus bacillus may remain implanted locally in environments favorable to the elaboration of specific toxin (cases 22 and 27). In addition, portions of splinters or other extraneous material may be missed (cases 6 and 10). Hence, although the surgical principles recommended for active treatment are to be followed in the prophylaxis of tetanus, the limitations of this form of therapy must be appreciated if prevention of the disease is to be effected.

Although the value of routine cleansing of superficial wounds and the desirability of applying various reliable antiseptics cannot be denied, it should be emphasized that penetrating injuries cannot be influenced by such procedures. The spores of the tetanus bacillus are too deeply implanted in the tissues to be affected by the aforementioned measures. Consequently, local medical treatment of puncture wounds must prove of slight, if any, value in prophylaxis (cases 3, 6, 7, 11, 14, 23, 26 and 27). It is of the utmost importance that the lay public be educated concerning the dangers attendant on inexpert and meddlesome treatment of apparently minor injuries (cases 22, 29 and 32).

The spores of the tetanus bacillus are widely distributed in nature, and their presence in street dust [38] is of great importance in civil practice. Some strains of the tetanus bacillus produce toxin, whereas others do not.[39] Furthermore, considerable variation in the capacity to produce toxin may be observed among the former. Hence, very mild lesions may cause severe clinical tetanus, whereas apparently serious injuries may not be followed by the disease. Physicians who have encountered numerous cases of tetanus are inclined to administer antitoxin for practically all injuries, whereas those with more limited experience are prone to withhold serum in the presence of minor wounds. At best, the decision is often in the nature of a gamble, and uncertainty as to the ultimate outcome may cause anxiety to all concerned. Nevertheless, the administration of tetanus antitoxin is indicated in the presence of lesions arising from the following causes: blank cartridge and powder injuries (Fourth of July, toy pistol, snapping mottoes [40]), penetrating wounds (bullets, nails, stabs), dirty lacerations, infected burns, self-induced or improperly performed abortions and injuries of any type in which contamination with soil, dust or animal dung might have occurred.

The amounts of serum recommended for prophylaxis have varied from levels of 1,500 to 20,000 units.[41] In the presence of injuries likely to cause tetanus, a prophylactic dose of at least 5,000 units [42] and under special conditions two to four times this amount, may be recom-

38. Gilles, E. C.: The Isolation of Tetanus Bacilli from Street Dust, J. A. M. A. **109**:484-486 (Aug. 14) 1937.

39. Fildes, P.: Tetanus: III. Nontoxic Variants of B. Tetani, Brit. J. Exper. Path. **8**:219-226 (June) 1927.

40. Commonly employed at birthday or other parties.

41. (*a*) Tetanusprophylaxie Fragen und Antworten, Chirurg **5**:644-646 (Aug. 15) 1933. (*b*) Present Status of Vaccination Against Tetanus, Foreign Letters (Paris), J. A. M. A. **111**:70-71 (July 2) 1938. (*c*) Meltzer, S. J.; Ochsner, A. J.; Lee, W. E.; Holman, O. J., and Brooks, C. D., in discussion on Gessner, H. B.: The Therapeutics of Tetanus, ibid. **71**:867-870 (Sept. 14) 1918. (*d*) Vener and others.[17a]

42. Fantus, B.: The Therapy of the Cook County Hospital: Therapy of Tetanus, J. A. M. A. **102**:2021-2022 (June 16) 1934. Vener and others.[17a]

mended.[43] If a delay of one or more days in the use of serum has already transpired when the patient is first seen, one should make the arbitrary assumption that the disease may already be in the incubation period, and a minimum dose of 20,000 units should be employed.[41c]

Certain disadvantages attend the use of tetanus antitoxin as a prophylactic agent. 1. The prompt administration of this material in the usually recommended amounts does not always prevent the later occurrence of tetanus.[44] Two instances of failure were encountered in my hospital material. The patient in case 21 (table 1) received an unstated amount on the day of a splinter injury; the dose was repeated five days later, and tetanus appeared fifty-four days after the second injection. The patient in case 7 was given 1,500 units of antitoxin twelve hours after stepping on a nail but had a mild form of tetanus eight days later. 2. Sensitivity to horse serum must be anticipated, and the rules proposed under the heading of serum therapy should be applied to the prophylactic use of antitoxin. However, despite all precautions, late serum reactions[45] may occasion marked discomfort and may temporarily incapacitate the patient. Acute anaphylactic shock,[46] at times fatal, may follow the first injections of serum. At times, distressing forms of neuritis or paralysis involving any of the body muscles[47] may occur as a result of serum sensitivity. 3. The transitory immunity[48] conferred, particularly by the 1,500 unit dose so

43. Footnote 41, *a* to *c*.

44. (*a*) Hanke, H.: Ueber Tetanus nach rechtzeitig ausgeführter Tetanusschützimpfung, Deutsche Ztschr. f. Chir. **242**:62-67, 1933; abstracted, J. A. M. A. **102**:574 (Feb. 17) 1934. (*b*) Vennat, H., and Micheleau, E.: A propos de deux cas de tétanos développés malgré l'emploi préventif du sérum, Gaz. d. hôp. **81**: 1719-1723, 1908. (*c*) Hertz, A. J.: Failure of Tetanus Prophylaxis, Ugesk. f. læger **100**:871-878 (Aug. 4) 1938. (*d*) Mosbacher, B.: Zur Serum- und operativen Prophylaxe des Tetanus, Arch. f. klin. Chir. **146**:41-63, 1927. (*e*) Graffagnino, P., and Davison, J. M.: Tetanus, New Orleans M. & S. J. **76**:311-315 (Jan.) 1924. (*f*) Boyd, J. S. K.: Active Immunization Against Tetanus, J. Roy. Army M. Corps **70**:289-307 (May) 1938. (*g*) Active Immunization Against Tetanus, Internat. M. Digest **32**:183-188 (March) 1938. (*h*) Footnote 41 *a* and *c*. Graves.[12a] Vener and others.[17a]

45. (*a*) Brown, H. H.: Active Immunization Against Tetanus, Brit. M. J. **1**:494-495 (March 6) 1937. (*b*) Boyd.[44f]

46. Gurd, F. B., and Emrys-Roberts, E.: Fatal Anaphylaxis Following Prophylactic Administration of Antitetanic Serum, Lancet **1**:763-764 (April 3) 1920.

47. Spaeth, R.: Unpublished data.

48. (*a*) Hempl, H., and Reymann, G. C.: Ueber das Verschwinden des Tetanusantitoxin aus dem Blut, Wien. klin. Wchnschr. **30**:235-236, 1917. (*b*) Lexen, E.: Ueber Wundstarrkrampf in der Praxis, München. med. Wchnschr. **80**:1117-1119 (July 21) 1933. (*c*) Dehne, R., and Hamburger, F.: Ueber das Verhalten artfremden Antitoxins in menschlichen Organismus, Wien. klin. Wchnschr. **20**:817-823, 1907. (*d*) McBryde, A.: Tetanus Immunization with Alum Precipitated Toxoid, South. M. J. **30**:565-567 (June) 1937. (*e*) Spaeth.[10g] Boyd.[44f] Hanke.[44a] Brown.[45a] Footnote 41 *b*.

commonly employed, leaves the patient unprotected after approximately ten to fourteen days. Hence, repeated injections become necessary in the presence of local infections.[49] In the event of reactivation of latent infections at a later date (trauma, local operations), reinjections of antitoxin are necessary. Likewise, subsequent injuries require the use of serum prophylaxis. 4. Tetanus antitoxin, in contrast with its toxoid, is relatively unstable, particularly if it is not kept under optimal conditions of refrigeration.[50] Deterioration of the antitoxin might in certain instances account for the failures encountered after prompt serum prophylaxis. Despite all the disadvantages listed, tetanus antitoxin should not be omitted when the conditions warrant its use.

The difficulties associated with the use of antitoxic serums could be reduced by induction of a relatively persistent form of active immunity. It has been pointed out that such a form of protection would have a wide field for use in both civil and industrial life and in all age groups of the general population.[51] Many investigations[52] have shown that

49. At times the number of injections indicated by the circumstances might be so great as to lead to the appearance of severe serum sickness, local necrosis (Arthus phenomenon), alarming anaphylactic shock, mental discomfort or problems of a purely financial character. With patients markedly sensitive to animal serums, most perplexing situations might arise. A further difficulty lies in the fact that reinoculations of antitoxin confer less enduring immunities than those obtained by the earlier injections (Brown[45a]; Dehne and Hamburger[45c]; Falchetti, E.: Recherches expérimentales vur l'immunisation antitétanique passive: mécanisme par lequel s'opère l'élimination rapide de l'antitoxine lors des réinjections de serum antitétanique, Compt. rend. Soc. de biol. **120**:592-595, 1935).

50. Hall, W. W.: Active Immunization Against Tetanus with Tetanus Toxoid, U. S. Nav. M. Bull. **35**:33-41 (Jan.) 1937.

51. (*a*) Fernan-Nuñez, M.: Tetanus Toxoid: Active Immunization Against Tetanus, Wisconsin M. J. **37**:21-24 (Jan.) 1938. (*b*) Hall.[50]

52. (*a*) Soldiers to Be Immunized Against Tetanus, Foreign Letters (Italy), J. A. M. A. **111**:462 (July 30) 1938. (*b*) The Prophylaxis of Tetanus, Foreign Letters (London), ibid. **111**:2504 (Dec. 31) 1938. (*c*) Hayden, R., and Hall, W. W.: Active Immunization Against Tetanus Using Alum-Precipitated Tetanus Toxoid, U. S. Nav. M. Bull. **36**:524-535 (Oct.) 1938. (*d*) Gold, H.: Active Immunization of Allergic Individuals Against Tetanus by Means of Tetanus Toxoid Alum-Precipitated Refined, J. Allergy **9**:545-550 (Sept.) 1938. (*e*) Gold, H.: Studies on Tetanus Toxoid: Active Immunization of Normal Persons with Tetanus Toxoid Alum-Precipitated Refined, J. A. M. A. **109**:481-484 (Aug. 14) 1937. (*f*) Jones, F. G., and Moss, J. M.: The Antitoxic Titres of Human Subjects Following Immunization with Combined Diphtheria and Tetanus Toxoids Alum-Precipitated, J. Immunol. **33**:173-181 (Sept.) 1937. (*g*) Jones, F. G., and Moss, J. M.: The Response of Human Subjects to an Injection of Tetanus Toxoid or Tetanus Alum-Precipitated Toxoid One Year After Immunization, ibid. **33**:183-190 (Sept.) 1937. (*h*) Ramon, G.: L'antitoxin tétanique et la prophylaxie du tétanos chez l'homme et chez les animaux domestiques, Presse méd. **44**: 1625-1628 (Oct. 17) 1936. (*i*) Lincoln, E. M.: Active Immunization of Human

(Footnote continued on next page)

active immunization against tetanus by means of toxoid is both safe and effective.[53] Its successful use in military [54] and civil [55] practice and also in animals [56] has removed it from the class of experimental procedures. Both Ramon [52h] and Cooke [33] have advised the routine use of combined tetanus-diphtheria toxoid in the immunization of children.

The present state of knowledge would indicate the employment of at least two, and preferably three, subcutaneous injections of 1 cc. of combined tetanus-diphtheria toxoid (refined) (alum precipitated) at two month to three month intervals. Such plurivalent injections are followed by antitoxic titers which are higher than those induced by single antigens.[52f, h] In the event of injury likely to cause tetanus, 1 cc. of tetanus toxoid may be injected instead of antitetanic serum, provided the immunization program has already been completed.[57] Under all other circum-

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Beings with Tetanus Toxoid, Proc. Soc. Exper. Biol. & Med. **30**:1241-1243 (May) 1933. (*j*) Bergey, D. H., and Etris, S.: Immunization of Humans with Alum-Precipitated Tetanus Toxoid, Am. J. Pub. Health **24**:582-586 (June) 1934. (*k*) Bergey, D. H.: Active Immunization Against Tetanus Infection with Tetanus Toxoid, J. Infect. Dis. **55**:72-78 (July-Aug.) 1934. (*l*) Sacquépée, E.: Immunisation contre le tétanos par l'emploi simultané de sérum et d'antitoxine antitétaniques, Paris méd. **1**:491-494 (June 3) 1933. (*m*) Ramon, G., and Lemétayer, E.: Sur la valeur et la durée de l'immunité conféré par l'antitoxine tétanique dans le vaccination du cheval contre le tétanos, Compt. rend. Acad. d. sc. **202**:1465-1466 (April 27) 1936. (*n*) Bergey, D. H., and Etris, S.: Tetanus Toxoid in Prophylaxis Against Tetanus, J. Infect. Dis. **53**:331-336 (Nov.-Dec.) 1933. (*o*) Cowles, P. B.: Tetanus Immunization, Yale J. Biol. & Med. **9**:409-416 (May) 1937. (*p*) Sneath, P. A. T., and Kerslake, E. J.: Persistence of Tetanus Antitoxin in Man Following the Administration of Active Immunization, Brit. M. J. **2**:290-291 (Aug. 17) 1935. (*q*) Active Immunization Against Tetanus, Internat. M. Digest **32**:183-188 (March) 1938. (*r*) Otten, J., and Hennemann, I. P.: Combined (Simultaneous) Immunization Against Tetanus, J. Path. & Bact. **49**:213-229 (July) 1939. (*s*) Cooke.[33] Boyd.[44f] McBryde.[48d] Brown.[45a] Hall.[50] Fernan-Nuñez.[51a] Footnote 41 *b*.

53. Toxoid apparently has an antitoxin-stimulating property not characteristic of natural toxin (Boyd [44f]; McBryde [48d]; Hayden and Hall [52c]). Its injection creates a permanent reacting mechanism, presumably in the reticuloendothelial system [44f] which causes the appearance of significant amounts of antitoxin when stimulated later by further doses of antigen (Cooke [33]; McBryde [48d]; Sneath and Kerslake [52p]; footnote 52 *q*; footnote 41 *b*; Hall [50]; footnote 52 *e*, *g*, *h* and *m*) or possibly by infection with tetanus bacilli (McBryde [48d]; footnote 52 *q*; Brown [45a]; Hayden and Hall [52c]). The production of this basal immunity is a slow process which requires several months to develop in response to injections given in the manner advised (Cooke [33]; Sneath and Kerslake [52p]).

54. Boyd.[44f] Footnote 41 *b*. Footnote 52 *a* to *c*.

55. Cooke.[33] Boyd.[44f] McBryde.[48d] Cowles.[52o] Sneath and Kerslake.[52p] Fernan-Nuñez.[51a] Footnote 52 *d* and *e*. Brown.[45a]

56. Footnote 52 *m* and *n*.

57. Cooke.[33] McBryde.[48d] Sneath and Kerslake.[52p] Hall.[50] Fernan-Nuñez.[51a] Footnote 52 *a*, *h*, *k* and *m*.

stances, the routine use of antitetanic serum is indicated.[58] In general, one may anticipate an adequately protective level of antitoxin within a week or less after the follow-up dose of toxoid.[59] The antitoxic titers induced by these subsequent injections of toxoid are stated to be far greater than those observed after the use of 1,500 units of antitetanic serum.[60]

Studies on horses and on human subjects [61] would indicate that the protection conferred by tetanus toxoid lasts at least several years and, with adequate reimmunizing injections, possibly a lifetime. Ramon [52h] recommended a reimmunization injection after one year and in certain instances every five years. Fernan-Nunez [51a] advised annual inoculations for workers constantly exposed to injuries likely to cause tetanus.

In general, reactions have been relatively mild.[61a] In the British army [45a] the inconvencience has been found to be so slight that the injections have been given during the height of the training season. McBryde [48d] found that all the children given injections were able to continue at school during the course of the injections. No more reactions were encountered with the use of combined diphtheria-tetanus toxoid than with the diphtheria toxoid alone.[62] Less than 10 per cent of the inoculated subjects may have slight soreness of the arm about the sites of injection.[48d] The local induration following intramuscular injections disappears in approximately forty-eight hours but lasts longer if the toxoid is given subcutaneously.[50] Occasionally, general malaise accompanied by slight elevations in temperature [50] or acute allergic reactions [63] may be encountered.

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58. The simultaneous injections of tetanus antitoxin and toxoid have been advised under the following circumstances: hemorrhage,[41b] poor health or the presence of other diseases of a debilitating nature [52p] or the occurrence of injuries which would justify the assurance of immediate protection (Boyd [44f]; footnote 41 *b*). In similar fashion, if the active immunization program has been carried out either incompletely or not at all, both serum and toxoid have been recommended in the form of two separate injections at the time of injury, the toxoid series to be finished in the usual manner (footnote 52 *d*, *h* and *k*). The theory underlying all the foregoing proposals is that passive immunization does not interfere with the development of antitoxin in response to toxoid (Boyd [44f]; Hall [50]). Since recent evidence [52r] indicates that passive immunization with antitetanic serum does impede the action of toxoid, the simultaneous use of toxoid and antitoxin cannot be recommended until more carefully controlled studies have been reported.

59. Cooke.[33] Hall.[50] Footnote 52 *c* and *d*.

60. Cooke.[33] Jones and Moss.[52g] Footnote 52 *q*.

61. Boyd.[44f] Hall.[50] Ramon.[52h] Ramon and Lemétayer.[52m]

61a. McBryde.[48d] Brown.[45a] Hayden and Hall.[52c]

62. Cooke.[33] Ramon.[52h]

63. Cooke, R. A.; Hampton, S.; Sherman, W. B., and Stull, A.: Allergy Induced by Immunization with Tetanus Toxoid, J. A. M. A. **114**:1854-1858 (May 11) 1940.

SUMMARY AND CONCLUSIONS

Up to June 1933, patients with tetanus admitted to the University Hospitals at Iowa City had been given general ward care, antitoxin in repeated doses by the intrathecal route in combination with other routes, radical surgical care of the local lesions and variable degrees of attention to sedative therapy. Since the aforementioned date a new routine has been followed. This has consisted of systematic sedation with avertin with amylene hydrate and/or sodium amytal, a single intravenous or intramuscular injection of 10,000 to 82,000 units of antitoxin, conservative surgical therapy and careful general management, with emphasis on constant nursing care, efforts to prevent pneumonia and maintenance of an adequate fluid and caloric intake. Thirty-three patients have been treated by the older methods and an equal number by the newer technic.

Comparison of the two series of patients in terms of both the severity of the tetanus and the incidence of complications indicated that in the new group the condition was more severe than in the old. Although the total mortality rates showed a difference of only 9 per cent in favor of the newer treatment, consideration of only the cases of moderate and severe involvement pointed to a significant reduction in mortality following the more recent method of management. Likewise, the advantages of the newer routine were apparent when the comparison of results was limited to the groups in which death was most likely to occur, namely, the patients with moderate to severe involvement admitted for treatment during the first four days of the disease after incubation periods of ten days or less.

Twenty-one of 45 patients with fever died, whereas no deaths occurred among 21 with normal temperatures. The cause of the fever, rather than its level, was of prognostic significance, as was revealed by the gravity of pneumonic complications.

Although at least 90 per cent of all deaths occur during the first ten days of the disease, later fatalities may be precipitated by complications (particularly pneumonia) or by causes not essentially related to tetanus.

The prompt use of antitoxin is recommended for all patients with tetanus, regardless of the clinical picture or the duration of the disease. The frequent absence of local lesions which may be incriminated and the possibility of atypical modes of onset justify the prompt administration of antitoxin even when the diagnostic data are inconclusive.

The intrathecal administration of antitoxin is to be condemned. Its use is based on an erroneous conception of the pathogenesis of tetanus. Intrathecal serotherapy may contribute to a fatal outcome by causing excitement, serum meningitis and possibly cerebral or medullary edema.

The intravenous, and under special circumstances the intramuscular, route is recommended for routine use.

On the basis of titration studies and clinical observations, a routine dose of 60,000 units of antitoxin is proposed for patients admitted for treatment during the first five days of the disease and a dose of 40,000 units for mildly to moderately ill patients first treated later. The optimal dose of antitoxin has not yet been determined.

A program is outlined for the prevention and treatment of reactions to antitoxin.

For patients with active tetanus, surgical treatment is not an emergency procedure and is of relatively secondary importance. Radical operation is justified only when a structure is already hopelessly destroyed. Treatment of wounds with oxidizing or other solutions may facilitate drainage and healing but cannot destroy the tetanus bacilli present locally.

All measures, specific and otherwise, ordinarily employed in the treatment of pneumonia should be used when this complication occurs in a patient with tetanus.

Tetanus may occur despite local surgical care, the application of antiseptic agents or the prompt injection of specific antitoxin in the doses ordinarily recommended. Depending on the circumstances, the dose of antitoxin may be increased to 5,000 or even to 20,000 units.

Because of the numerous insurmountable difficulties encountered in the prophylaxis of this disease, active immunization with tetanus toxoid is recommended for routine use.

Dr. Philip C. Jeans gave support and criticism which made this study possible.

9030 South Bell Avenue.

TO THE BABY DOCTOR

WILLIAM E. B. HALL, M.D.
DENVER

My world is the science of medicine. Among my test tubes, serums, lights and microscope, I find happiness: a guardian at a crossroads, a guide along the misted road to health. Yet in my daily rounds there sometimes comes an hour when I feel an emptiness. The sense of sacred missions that fire the priest and preacher, the teacher and the nurse seems strangely lacking, for mine is not the laying on of hands. Then it is that I must go to other courts—where children laugh, unconscious of the horror of their twisted bodies; where fevers burn and wasting illness stalks from cot to cot. There it is I see him, between the beds, in whitened gown, so kindly, calm and smiling—the baby's doctor. His gentler hands will hold some poor wee human mite, whose whispered breath scarce dares return to tortured lips. With defter eye and touch he reads its tale, and swiftly then there fly those hands and feet and stranger means to aid. Soon there comes a cooler blush to sunken cheeks, a gentle breath, a laugh, or little limbs no longer turned in pain—and tears and happy smiles to those who just a little while before had known the blackest fears, had prayed, had hardly dared to hope. It's like some miracle. And standing there, I strangely feel—a holy Presence.

His work has always been like mine, a science, relentless tests or gifted formulas. But may I add to this, a knowing mind and kindly heart—and the hands of Him. For I believe that He comes closest here on earth in the baby doctor.

3800 East Colfax.

News and Comment

GENERAL NEWS

The following physicians have been certified by the American Board of Pediatrics since the last report:

Mary Adams, Riverside, Conn.; Horst Albert Agerty, Merion Station, Pa.; Herbert C. Archibald, Salinas, Calif.; Lawrence Charles Bachmann, Pittsburgh; Sherod Marshall Billington, Seattle; Russell John Blattner, St. Louis; W. Warrick Cardozo, Washington, D. C.; Alice Drew Chenoweth, Rosemont, Pa.; Elizabeth Chickering, Washington, D. C.; J. Wallace Cleland, Lansdowne, Pa.; Edwin Revere Cole, Sacramento, Calif.; James Meredith Coleman, Austin, Texas; Richard L. Day, New York; William C. Deamer, San Francisco; Robert H. Detwiler, Boston; James Joseph Donahue, East St. Louis, Ill.; Richard A. Downey, Buffalo; Lucius Elkanah Eckles, Topeka, Kan.; Herbert L. Elias, Rockville Center, N. Y.; H. H. Finlay, Wilkinsburg, Pa.; Frederick R. Fischer, Spokane, Wash.; Gerald Robert Fisher, Colorado Springs, Colo.; S. Howard Fleri, Brooklyn; C. Dixon Fowler, Atlanta, Ga.; John Edward Franklin, New York; Robert Clarence Fredeen, Kansas City, Mo.; Emily Gardner, Richmond, Va.; Isaac F. Gittleman, Brooklyn; Moe Goldstein, Forest Hills, N. Y.; Scott H. Goodnight, Portland, Ore.; Milton M. Greenberg, Washington, D. C.; Margit Helga Grytbak, Seattle; James P. Hanner, Atlanta, Ga.; L. Martin Hardy, Chicago; Edward Harshaw Jr., Yeadon, Pa.; George V. Herrman, Kansas City, Mo.; Helen Hopkins, Los Angeles; William Allen Howard, Washington, D. C.; Betty Huse, Washington, D. C.; Robert Lawrence Jackson, Iowa City; F. Craig Johnson, Denver; Margaret Holden Jones, Cheyenne, Wyo.; Frederick B. Joy, Seattle; Isaac W. Karlin, Brooklyn; Haddow M. Keith, Rochester, Minn.; Bruce A. Knickerbocker, Dallas, Texas; Louis M. Kochin, Pittsburgh; Pearl Vivian Konttas, Santa Rosa, Calif.; Robert Spencer Leet, Oakland, Calif.; Arthur Lesser, New York; Joseph L. Lewis, Boston; Harry Lowenburg Jr., Philadelphia; George Maksim, Petoskey, Mich.; Rocco J. Martoccio, Utica, N. Y.; Paul Francis McAlenney Jr., New Haven, Conn.; Jean McAlister, Greensboro, N. C.; Kenneth W. A. McLeod, Lapeer, Mich.; Donald Norman Medearis, Kansas City, Kan.; Ernst R. Moeller, Denver; Robert A. Moore, Charlotte, N. C.; Gertrude Halero Brown Nicolson, New York; Edward Thomas O'Donnell, Wilmington, Del.; Robin M. Overstreet, Eugene, Ore.; Jean Pakter, New York; Karl Francis Pelkan, San Jose, Calif.; John Robert Phillips, Allentown, Pa.; Jacob David Pinson, Philadelphia; Howard G. Rapaport, New York; Henry Rascoff, Brooklyn; Willard B. Rew, Yakima, Wash.; Louis S. Robins, Chicago; Harold A. Rosenberg, Flushing, N. Y.; Arthur H. Rosenblum, Chicago; Isadore Rosmovsky, Staten Island, N. Y.; Eli Rubenstein, Bayonne, N. J.; Michael Schuman, New York; Isadore B. Silber, Cleveland; Joseph McBride Sloan, Corpus Christi, Texas; Leslie A. Smith, Ogden, Utah; Frank Marion Sprague, Boise, Idaho; Charles A. Tompkins, Omaha; H. Milton Van Dyke, Long Beach, Calif.; Myron Ezra Wegman, Baltimore; Samuel Bernard Weiner, New York; Louis Ernest Weymuller, New York; Henry Booth Wightman, New Rochelle, N. Y.; Simon A. Wile, Chicago; Abbott L. Winograd, Nashua, N. H.; C. Michael Witzberger, New York; Leon Z. Wolpe, Los Angeles; Charles Louis Wood, New York; Tyree C. Wyatt, Syracuse, N. Y., and Charles Andrew Wylie, San Bernardino, Calif.

Report of Commission on Graduate Medical Education.—Important developments in the hospital internship, the hospital residency and the postgraduate educational opportunities for physicians in practice were suggested by the Commission on Graduate Medical Education, whose final report was published on June 25. The commission, which was organized by the Advisory Board for Medical Specialties on Dec. 4, 1937, is now bringing to a close its three year study program. Its work has been financed by national foundations and interested professional organizations.

The internship, suggests the commission, should be considered as a basic preparation for the practice of medicine. It should round out and give practical application to the medical school course and hence should be closely allied to undergraduate medical education. It should prepare young physicians adequately to begin general family practice and should provide them with the essential preparation necessary to undertake further study leading to the practice of a specialty. It should not attempt to train men for the specialties directly, and therefore the intern should not be given training in the detailed technics of the specialties.

To prepare the intern for general practice, he should have experience in internal medicine, pediatrics, obstetrics and gynecology, surgical diagnosis, minor surgery and treatment of emergencies. Special attention in these fields should be given to preventive medicine and the care of chronic diseases, conditions of the aged and functional disturbances. The whole atmosphere should be educational, and the intern should learn by example as well as precept.

The residency is defined by the commission as a prolonged period of study in one of the special fields which can be properly classed as graduate education, whether an advanced degree is granted or not. The commission warmly supports the recommendation of the specialty boards that adequate attention be given during the residency to the basic sciences as they relate to the various specialties. It suggests practical ways by which hospitals may provide this basic science training in their own laboratories or through arrangements with medical schools. The report suggests that there is danger that too many residencies may be developed and stresses that, in the best interests of the patient, high quality of teaching in the residency is now more important than a large increase in the number of residencies. The essentials of a satisfactory residency are listed in some detail, although the commission takes pains to point out that it does not wish to standardize residencies or put them in a strait jacket.

Postgraduate education the commission defines as study intended to keep a physician abreast of his chosen field of practice but not intended to equip him to enter a new field. Separate and clearly defined types of work are recommended for general practitioners and for specialists. While there has been a marked and rapid increase in interest in the field of postgraduate medical education, there is still need for its further extension and for improvement in the type of opportunities offered. The report points out the advantages and disadvantages of the various types of training now provided.

The effect of the work of the specialty boards on the practice of medicine is discussed in the report, which points out that these boards have provided a well defined yardstick for measuring an individual physician's competence in his specialty. Men in the specialties have been certified so rapidly that it soon will be possible for the great majority of the people of this country to have access to the services of certified specialists.

The entire report stresses the value of adequate training and points out that this will be reflected in improved care of patients.

DEATHS

Dr. Alfred James Scott Jr., one of the early pediatricians of Los Angeles, died on April 17, at the age of 58. Dr. Scott was active in medical society work and will be missed by all pediatricians. He was always willing to do his share of the work and was always kindly in doing it.

According to an announcement in one of the French publications, Dr. Eugéne-Charles Apert, of Paris, died recently at the age of 71. Dr. Apert was one of the most distinguished of the French pediatricians, and his loss will be deeply felt.

PERSONAL NEWS

Appointment Announced.—Dr. Hugh L. Dwyer, of Kansas City, has been made health commissioner of Kansas City.

Degrees Awarded.—Dr. T. B. Cooley, of Detroit, was given the honorary degree of Doctor of Science by the University of Michigan.

Dr. Samuel McClintock Hamill, of Philadelphia, has received the degree of Doctor of Science from the University of Pennsylvania.

Abstracts from Current Literature

Biochemistry, Bacteriology, and Pathology

MOLD SPORE CONTENT OF THE AIR IN BOSTON WITH REFERENCE TO ATOPIC SENSITIVITY. H. N. PRATT, J. Pediat. **14**:234 (Feb.) 1939.

Petri dishes containing Sabouraud's medium were exposed to the outside air for a half hour each day for fourteen months. Alternaria, Hormodendrum fontoynonti and non-spore-bearing molds were observed to increase in quantity gradually during the spring months, to increase rapidly during July, August and September and to taper off during October and November. Aspergillus, Penicillium and other air-borne molds failed to display a seasonal incidence.

Twenty-five per cent of 177 children suffering from asthma and hay fever reacted strongly to Alternaria extracts, on being tested intracutaneously. A much smaller number reacted to other molds. Reagins to Alternaria could easily be demonstrated in the serums of 92 per cent of 26 children chosen at random from among those giving strong cutaneous reactions to Alternaria. Reagins to other molds were less frequently present. When the effect of coexisting sensitivity to pollen is taken into account, the seasonal incidence of symptoms among those patients giving strong cutaneous reactions to molds corresponds closely to the seasonal variations of mold spores in the outdoor air. During 1937, 34 patients were treated with mold extracts. Twenty-three of these patients also received pollen therapy. Of the 11 receiving only mold treatment, 9 obtained marked relief and only 2 failed to benefit. FROM AUTHOR'S SUMMARY (RAUH, Cincinnati).

INFLUENCE OF SODIUM CHLORIDE ON THE ACTIVITY OF THE AMYLASE: ENZYMES OF CHILDREN. G. TOMMASEO, Riv. di clin. pediat. **37**:897 (Nov.) 1939.

The mean sodium chloride content of the saliva of 9 infants was 2.07 Gm. per liter (maximum, 2.3 Gm.; minimum, 1.82 Gm.); this is higher than the mean for 5 adults (1.33 Gm.). The mean sodium chloride content of the pancreatic juice of 10 infants was 8.45 Gm. per liter (maximum, 11.4 Gm.; minimum, 5.79 Gm.).

The amylase potency was determined in vitro by adding the juice to a starch solution. The amylases of saliva and pancreatic juice were found to vary in potency in different infants and in the same infant on different days. The age of the infant or its diet (breast or bottle) was not a factor in the potency of the amylase in its saliva.

The optimum amount of sodium chloride for amylase activity of the saliva was 4 Gm. per liter; with 7 Gm. per liter the activity fell to a degree equivalent to that in saliva with no sodium chloride. While the activity was increased, in that the reaction of the saliva in changing starch to maltose was hastened, the ultimate percental change from adding salt was not increased after three hours.

The optimal sodium chloride concentration in pancreatic juice as to amylase activity was 9 to 12 Gm. per liter. Dialysis of pancreatic juice to reduce its salt content resulted in diminution of amylase potency only in proportion to the reduction of the sodium chloride.

HIGGINS, Boston.

Metabolism; Infant Feeding; Milk and Other Foods

NATURE OF VIRUCIDAL VACCINIAL ANTIBODIES IN HUMAN MILK AND THE QUESTION OF THEIR TROPHOGENIC TRANSFERENCE. F. WEISS, Ann. pædiat. **152**:193 (Jan.) 1939.

Virucidal antibodies against vaccinia can as a rule be demonstrated in colostrum and in mother's milk proper if they can be found in the maternal blood serum. Trophogenic transmission of these antibodies in man, in contrast to the placental, takes place only exceptionally and to a small extent. The priority of placental over trophogenic transmission seems to be general in man, since it extends equally to immune bodies against scarlatina, diphtheria, tetanus and vaccinia.

FROM AUTHOR'S SUMMARY.

THE SULFUR AND ALBUMIN METABOLISM OF THE BREAST-FED AND OF THE ARTIFICIALLY FED INFANT. S. BLAZSO, Ann. pædiat. **152**:302 (Feb.) 1939.

Cow's milk contains the same amount of organic sulfur as mother's milk, although its protein content is twice as great.

Investigations of the sulfur metabolism of the breast-fed child show that the protein sulfur is almost completely absorbed and that up to 90 per cent of it is retained. Since the proportion of protein retained (as estimated on the nitrogen-balance) is lower, it may be assumed that the growing organism retains primarily the protein sulfur, i. e., the part of the protein molecule which is most valuable for its purposes.

The degree of the absorption of sulfur does not alter during mixed feeding, but the retention is 10 per cent less.

The sulfur absorption of infants fed on cow's milk only is still the same, while the amount of sulfur retained is even smaller than in the previous group.

On the basis of these experiments a hitherto unknown difference between natural and artificial feeding could be ascertained. The infant cannot utilize the sulfur-containing amino acids of cow's milk proteins as well as it can those of mother's milk. There is a qualitative difference between the protein metabolism of the artificially fed child and that of the naturally fed child.

FROM AUTHOR'S SUMMARY.

INFLUENCE OF THE FEEDING OF LACTIC AND CITRIC ACID MILK ON THE ACID BASE RELATIONSHIP IN THE INFANT. E. RODLER, Ann. pædiat. **153**:207 (July) 1939.

The metabolism of infants was investigated while they were on lactic acid milk and later while they were on citric acid milk. The lactic acid period was compared with the citric acid period in the same infant. The following points were noted:

1. During the lactic acid period there was an increased excretion of organic acids as compared with the citric acid period.

2. During the lactic acid period there was a tendency toward decreased excretion of total urinary phosphates.

3. During the lactic acid period there was also a marked tendency toward retention of fixed bases, while in the citric acid period the excretion of these substances was augmented.

4. The Mainzer coefficient does not differ substantially during the two periods. The newly evolved quotient—100 × organic acids over cations—however, gives lower values during the use of citric acid milk and higher ones during the lactic acid milk period.

The abovementioned observations lead one to suppose that if a quantity of milk is acidified with equal amounts of lactic and citric acid, respectively, the influence of citric acid on the metabolism of the infant tends more toward an

inorganic, and the influence of lactic acid more toward an organic, acidosis. The acidosis, however, was in each case fully compensated. It is noteworthy that these differences result from well metabolizable acids.

The urinary anions and cations were charted, and an excess of the latter was found. This excess was larger during the citric acid period. Thus certain anions must have escaped analysis, probably some of the organic acids. These acids not found during analysis were excreted to a greater extent during the citric acid period, but citric acid itself was not among them.

FROM AUTHOR'S SUMMARY.

MORSELS OF CASEIN AFTER INGESTION OF RAW COW'S MILK. S. WOLFF, Ann. pædiat. **154**:54 (Oct.) 1939.

Being on the question of casein curds in the stools of sucklings, the case of an infant is reported who vomited and passed in his bowel motions, respectively, two structures (shown natural size in a picture) which consisted of pure casein. The vomited piece represented a cast of the stomach, while in the other piece the haustra of the bowel could be easily recognized. Repeated experiments with raw milk diluted one-half and with protein milk yielded negative results, while each time after a feeding of undiluted raw milk large lumps of casein were found in the stools. The size of the structures mentioned is particularly striking.

FROM AUTHOR'S SUMMARY.

Vitamins; Avitaminoses

EFFECT OF AVITAMINOSIS A ON THE HUMAN BLOOD PICTURE. O. A. ABBOTT C. F. AHMANN and M. R. OVERSTREET, Am. J. Physiol. **126**:254 (June) 1939.

The subjects studied were college students, women and rural school children. For various reasons these persons had been living on restricted diets for periods which varied from a few months to many years.

The children had lost the alertness of health and were listless and inattentive, but conjunctivitis was the most outstanding defect in this group. In a few cases the ocular condition had progressed so far that there was actual involvement of the cornea and the conjunctiva appeared salty. The skin had become dry and desquamated. These flaky areas were particularly noticeable on the back of the forearm, the upper part of the arm near the tip of the shoulder, on the calves and across the chest.

Many of the children had no subcutaneous fat, so that the skin on the face was shriveled and dry. The hair was also dry, had lost its normal gloss and appeared bleached and lifeless.

A study was made of the differential leukocyte counts of 157 subjects whose diets and symptoms indicated a deficiency of vitamin A. The characteristic changes, which were constant in the blood pictures of these subjects, were mild leukopenia, a decrease in the number of polymorphonuclear neutrophils, a relative increase in the number of large lymphocytes with a corresponding drop in that of small lymphocytes, the occurrence of degenerate cells and an increase in the number of immature cells.

From this work it was concluded that the differential leukocyte count is of value in diagnosing a deficiency of vitamin A in man. NOURSE, Cleveland.

RACHITIC STUDIES: II. THE VALUE OF IRRADIATED EVAPORATED MILK IN THE PREVENTION OF RICKETS IN PREMATURE, WEAKLING, AND NORMAL FULL TERM INFANTS. E. W. MAY and T. M. WYGANT, Arch. Pediat. **56**:356 (June) 1939.

The infants were divided into two major groups—those fed on irradiated evaporated milk (the "prophylactic" group) and those fed on nonirradiated evaporated milk (the "control" group). They were all fed according to the same method.

In none of the 51 normal, full term infants in the "prophylactic" group did rickets develop, while in the "control" group (33 full term infants) rickets developed in 17 by the seventh month of life. The average length of time for the development of rickets was five months.

In none of the 20 infants in the weakling group that were fed irradiated evaporated milk did rickets develop. In 13 of the 20 weakling infants in the "control" group rickets developed before the age of 6½ months.

In 2 of the 18 premature infants in the "prophylactic" group rickets developed. The rachitic process in 1 infant was mild and healed spontaneously with the continuance of irradiated evaporated milk feedings. Rickets developed in all of the 17 infants in the "control" group before the eighth month. The average age when signs of rickets appeared was 4½ months. ORR, Buffalo.

XEROPHTHALMIA IN A SYPHILITIC INFANT ELEVEN MONTHS OF AGE. M. E. HURMUZACHE, E. TRIANDAF and I. NICHITA, Bull. Soc. de pédiat. de Iasi **9**:13, 1938.

Because of feeding difficulties, the infant in question received a diet moderately low in fat. The authors felt that the syphilis interfered in some way with the absorption of vitamin A. However, on a liberal allowance of vitamin A the xerophthalmia disappeared. LESLIE, Evanston, Ill.

VITAMINS AND THE NERVOUS SYSTEM. A. AUSTREGESILO, Confina neurol. **2**:185, 1939.

Austregesilo discusses the direct and indirect relationships of vitamins, hormones and the vegetative nervous system, particularly the role of vitamin deficiencies in nervous and psychic disorders. In both beriberi and experimental B_1 avitaminosis he found involvement of the central as well as of the peripheral nervous system, with neuronophagia in the cerebral cortex. Vitamin B complex, particularly the B_1 factor, and vitamin C are closely related to the dynamics of the nervous system, and the author has observed in patients with scurvy polyneuritis similar to that observed in patients with deficiency of vitamin B_1.

DE JONG, Ann Arbor, Mich. [ARCH. NEUROL. & PSYCHIAT.]

AVITAMINOSIS A IN THE HUMAN SPECIES. V. BAPTISTA, Pediat. prat. **9**:412 (Sept.-Oct.) 1938.

Baptista gives a detailed and scholarly review of the literature on vitamin A. DIETRICH, Beverly Hills, Calif.

VITAMIN B_1 IN THE TREATMENT OF ALIMENTARY EDEMA IN INFANTS. A. KOLLMANN, Arch. f. Kinderh. **117**:64 (May) 1939.

Kollmann gave various vitamin B_1 preparations to 10 infants with malnutrition associated with edema of various degrees. After diuresis of several days' duration, the infants began to gain steadily. Another 8 infants with malnutrition but no demonstrable edema were given vitamin B_1, and after a short early increase in weight, and then a decrease which continued for a number of days, there was a definite steady increase in weight, accompanied by improvement in the general condition. HANSEN, Minneapolis.

VITAMIN D AND THE BONE FORMATION. R. NICOLAYSEN, Acta pædiat. **24**: 368, 1939. VITAMIN D AND BONE FORMATION IN RATS. R. NICOLAYSEN and J. JANSEN, ibid. **23**:405, 1939.

In both short and long term experiments on rats involving privation of vitamin D, the density of the calcification of bone appeared to be governed solely by the amount of calcium and phosphorus absorbed into the body. Specif-

ically, the influence of vitamin D appeared to be insignificant with respect to the bone ash. However, histologic examination indicated that vitamin D has, directly or indirectly, an effect on the architecture of the bones. McCUNE, New York.

TREATMENT OF RICKETS BY ORAL ADMINISTRATION OF SINGLE MASSIVE DOSES OF CONCENTRATED VITAMIN D_2. A. R. MEYER, Acta pædiat. **24**:373, 1939.

Harnapp's *Stosstherapie* was used with gratifying success in 12 cases of active rickets. In agreement with the German reports, serum calcium and phosphorus rose rapidly, sometimes to levels higher than normal. The hypercalcemia was of short duration; the elevation of phosphorus occasionally lasted for some time. Mildly increased phosphatase quickly returned to normal; high levels remained unchanged until long after clinical and roentgen evidence indicated cure of the disease.

The indications for this type of treatment are enumerated, and the feasibility of employing a similar technic in prophylaxis is brought up.

McCUNE, New York.

EARLY DIAGNOSIS OF RICKETS BY ROENTGEN EXAMINATION. F. KNUTSSON, Acta pædiat. **24**:403, 1939.

Systematic roentgen examinations were made of the wrist, ankle and costochondral articulations of each premature infant during the first year of life. Rachitic changes were found in 36 infants; in 10 of these the pathologic roentgen findings occurred exclusively in the ribs. In 18 infants the abnormalities were demonstrated in the ribs before they were apparent elsewhere, and in 17 infants they occurred simultaneously in the ribs and in the distal metaphysis of the ulna. In mild rickets that healed rapidly the costal lesion was unique, the other metaphyses remaining free of any alteration. Well marked cupping with considerable deformity was found to be the first peculiarity in the ribs. In the ulna and fibula the first manifestation of rickets was less conspicuous cupping of the end of the metaphysis, accompanied by some loss of definition in this region. In the tibia the earliest sign was frequently spur formation at the margin of the metaphysis, followed later by cupping.

A full description is supplied of the roentgen technic employed in examining the ribs. McCUNE, New York.

INVESTIGATIONS OF THE INFLUENCE OF LIQUID PETROLATUM ON THE ALIMENTARY RESORPTION OF VITAMIN A IN MAN. O. ANDERSEN, Acta pædiat. **24**:422, 1939.

Animal experiments have demonstrated that oral ingestion of liquid petrolatum effectively hinders intestinal absorption of carotene and, to a lesser extent, of vitamin A. Similar observations have been made in man. The author's experiments consisted in daily administration of 7,000 international (equivalent to U. S. P. XI) units of vitamin A to human subjects before, during and after their ingestion of liquid petrolatum. In this way it was demonstrated that the oil caused a consistent loss of vitamin A in the feces, although in no case was more than 25 per cent of the ingested vitamin lost. The average waste was about 20 per cent. This effect was apparently due to the solubility of the vitamin in oil, since the use of nonoily cathartics did not increase the excretion of vitamin A. In a single patient suffering from sprue, the administration of vitamin A was regularly followed by an increase in the amount of the substance excreted in the stools.

It is recommended that liquid petrolatum be used regularly only if the patient's intake of vitamin A is ample. The oil should be given as far from mealtime as is possible. It should be used sparingly, if at all, when alimentary resorption is impaired. McCUNE, New York.

Hygiene; Growth and Nutrition; Public Health

A Consideration of Race and Sex in Relation to the Growth and Development of Infants. E. C. Dunham, R. M. Jenss and A. U. Christie, J. Pediat. **14**:156 (Feb.) 1939.

Race and sex should be taken into consideration in studying the growth and development of the infant. Of 2,923 live infants born, 50 per cent of the Negro girls weighed less than 3,003 Gm., and 50 per cent of the Negro boys weighed less than 3,182 Gm. For the white infants, the corresponding weights were 3,340 and 3,457 Gm. The white infants weighed more on the average than the Negro infants, and for each race group the average boy weighed more than the average girl. Six per cent of the white boys and 14 per cent of the Negro girls weighed less than 2,500 Gm. This is of interest in the study of premature infants, for when a birth weight of 2,500 Gm. or less is taken as a criterion of permaturity, more than twice as many Negro girls as white boys are included. Osseous development also varies with sex and race. Roentgenograms to determine the presence or absence of the center for the cuboid were taken of 498 infants within seventy-two hours after birth. The cuboid was present in the roentgenograms of infants weighing less than 2,500 Gm. in 15 per cent of the white girls, in 17 per cent of the Negro boys and in 37 per cent of the Negro girls; it was absent from the roentgenograms of all the white boys weighing less than 2,500 Gm. In the group weighing from 3,500 to 4,500 Gm. at birth, the center was present in the roentgenograms of 42 per cent of the white boys, of 59 per cent of the white girls, of 70 per cent of the Negro boys and of 75 per cent of the Negro girls. The center for the cuboid is present more frequently in newborn Negro infants than in newborn white infants of the same birth weight and within a given race group; it is present more frequently in the girls than in the boys. The development of the center for the cuboid is related to both the race and the sex of the infant.

Rauh, Cincinnati.

The Children's Bureau in the United States. G. Lessa, Bol. Inst. internac. am. de protec. a la infancia **13**:5 (July) 1939.

As a summary of his interesting and well reported work, the author states the principal functions of the Children's Bureau, which are: (1) to investigate, (2) to publish, (3) to demonstrate and (4) to encourage the organizations of the different states with financial or technical assistance. From Editor's Summary.

Infant Mortality in Bolivia. L. V. Sotelo, Bol. Inst. internac. am. de protec. a la infancia **13**:86 (July) 1939.

On the basis of a detailed report Sotelo studies the infant death rate of four Bolivian cities: La Paz, Oruro, Sucre and Santa Cruz. He describes the hygiene as very deficient, the available water as bad and the dwellings of the people as poor; in general, the common people are beset by ignorance, vice and alcoholism, and they consume "astonishing quantities of cocoa leaves."

In La Paz the infant death rate was 267 per thousand liveborn children (report for the year 1937); in Oruro, 214 per thousand (1937); in Sucre, 194 per thousand (an average of four years); in Santa Cruz, 118 per thousand (an average of four years).

Illegitimacy is also very high: in La Paz, 43 per cent; in Oruro, 46.54 per cent; in Sucre, 49 per cent; in Santa Cruz, 84 per cent.

The population of La Paz is thus composed: 27 per cent, Indian; 31 per cent, mixed breeds, and 42 per cent, white; with regard to mortality of the races the result is: Indian, 30.94 per cent; mixed, 64.86 per cent; white, 17.68 per cent.

The author studies in particular the conditions of the population in the vicinity of a tin mine. The workers dwell in camps around the mine. Salaries are low; milk, eggs, fresh vegetables and fruit are articles of luxury for the worker; all this explains the fact that the infant death rate reaches the incredible figure of 370 per thousand.

FROM EDITOR'S SUMMARY.

NORMAL DEVELOPMENT OF THE INFANT. E. BORSATTI, Arch. ital. di pediat. **6**:429 (Sept.) 1938.

In the pediatric clinic of the University of Padua, Italy, Borsatti made observations on the development of infants, using the anthropometric method.

He discusses the various methods used by earlier obervers, and the results they obtained, especially those of Viola, Variot, Mensi, Moggi, Pirquet and Baldwin. He then reports his own results, obtained in a study of 788 normal infants, taking into consideration numerous factors, and compares them as to sex, age, race, social status, heredity and type of feeding.

The article is interesting and valuable for the accuracy of the statistics and for the comparison of them with the earlier ones, none of which, however, are recent. It is a painstaking study of males and females at birth and at different ages up to 1 year as to weight, rate of growth, individual curves of gradual declines and height. He gives brachiskelous measurements, the relation between height and weight, skull circumferences, biparietal and fronto-occipital measurements, thoracic measurements at the fourth and at the tenth rib, and anteroposterior and transverse diameters of the thorax. He calculates the thoracic index and the thorocephalic index.

The long article is enriched by numerous graphs.

PREVITALI, New York.

AN INQUIRY INTO THE DOMESTIC ENVIRONMENT OF SO-CALLED UNDERWEIGHT SCHOOL CHILDREN. A. RUOTSALAINEN, Acta pædiat. **23**:315, 1939.

The author's earlier investigation of a group of 457 Finnish children classified as underweight with respect to height revealed that only 40 per cent of the subjects were really malnourished when classified according to the thickness of their subcutaneous fat. However, between 65 and 72 per cent of representatives of the same social class exhibited underdevelopment of their skeletal musculature. The present paper reports the results of an inquiry into the prevalence among these children of those factors that are commonly thought to be responsible for underweight, namely, lack of proper food, sleep, fresh air and sun, unhygienic and crowded living quarters and prematurity of birth. None of these circumstances could be demonstrated more commonly among the underweight children than among those whose relation of weight to height was normal. On the other hand, it did become apparent that the tall, thin children bore a close resemblance to one or the other of their parents. The tentative conclusion is drawn that in many cases so-called undernutrition is in reality a manifestation of a leptosomatic constitution and, as such, is the result of endogenous rather than exogenous causes.

MCCUNE, New York.

INFANT MORTALITY IN GÖTEBORG DURING THE LAST THIRTY YEARS. A. BRODIN, Acta pædiat. **24**:42, 1939.

During the period covered by Brodin's inquiry the total infant mortality in Göteborg, Sweden, has decreased dramatically, while the rate of death during the first few days of life has remained almost unchanged. Apparently, whatever has been accomplished in the way of antepartum hygiene is offset by the mounting proportion of primiparous births and by the increase of the average age of women at the time of the birth of the first child. The situation was found to be substantially the same in all classes of society. The contemporary problem is not one of medical therapeutics but a social and economic matter.

MCCUNE, New York.

WELFARE WORK FOR MOTHER AND CHILD. K. UTHEIM-TOVERUD, Acta. pædiat. **24**:116, 1939.

The author describes the gratifying results obtained by extending medical hygiene and prophylaxis into the rural community of Skedsmo, Norway.

McCUNE, New York.

STUDIES ON TWINS. G. SEVERIN and E. MANNHEIMER, Acta pædiat. **24**:137, 1939.

Severin and Mannheimer confirm the generally held opinion that comparison of fingerprints is of value in determining the identity or the nonidentity of twins. Also, the normal as well as the abnormal physical findings relating to the heart exhibit closer resemblance in the case of single ovum twins than in the case of twins of double ovum origin. Although monozygotic twins occasionally show virtually identical electrocardiographic tracings, on the whole no greater conformity exists between the tracings of single ovum twins than between those of dizygotic twins.

McCUNE, New York.

Prematurity and Congenital Deformities

DYSOSTOSIS CRANIO-FACIALIS (CROUZON). A. C. KRAUSE and D. N. BUCHANAN, Am. J. Ophth. **22**:140 (Feb.) 1939.

Krause and Buchanan discuss malformations of the head, the classification of such malformations and the symptoms, signs, prognosis and treatment of craniofacial dysostosis. They report the occurrence of craniofacial dysostosis or Crouzon's disease in a 2½ year old American boy. The symptoms were typical, and the diagnosis was confirmed by roentgen ray examination. There is no apparent record of this disease in the American literature. In spite of operative decompression of the cranium and right orbit there is "no reason to believe the prognosis will be favorable for either the eye, mentality, or life."

REESE, Philadelphia [ARCH. OPHTH.]

STUDIES OF HUMAN OVA. S. P. REIMANN and B. J. MILLER, Arch. Path. **27**:412 (March) 1939.

Five unfertilized ova were recovered from human fallopian tubes immediately after surgical removal and were studied for evidence of parthenogenesis. It has been suggested in the past that dermoid cysts, teratomas and certain hamartomas may have their origin from parthenogenetic activity of ova. No proof, however, has been reported in the literature that human ova are capable of parthenogenesis.

One ovum, following mechanical stimulation in a medium of human blood serum containing a minute trace of the ethyl ester of acetic acid, was observed to exhibit parthenogenetic activity, resulting in the extrusion of polar bodies and the formation of a deep cleft.

The authors conclude that the human ovum is capable of being artifically stimulated to parthenogenetic activity.

APPELBACH, Chicago.

THE PLACE OF DENTAL HYGIENE IN A MATERNAL AND CHILD HEALTH PROGRAM. K. F. LENROOT, J. Am. Dent. A. **26**:263, 1939.

"The maternal and child-health program and the program of services for crippled children under the Social Security Act have made possible considerable advance toward community-wide dental health programs for mothers and children. . . . The interdependence of the general health and dental health . . . is recognized by the dental profession and by federal and state official health agencies. Present funds available for public services to mothers and children are sufficient

only to make a beginning in demonstrating the need and the possibilities of working out a practicable program under competent technical direction and with the cooperation of professional organizations and private practitioners."

FROM AUTHOR'S SUMMARY.

THE IMMATURE NEWBORN. E. MEYNIER, Lattante **10**:427 (Nov.) 1939.

Data are recorded on the weight, height, feeding and mortality of 792 immature newborn infants at the Maria Victoria Hospital, Turin, Italy, between 1910 and 1936. Of these infants, 48.1 per cent were boys and 52.2 per cent were born of primiparous mothers; 13.2 per cent were twins. Of mature newborn infants 52.9 per cent were boys and 40.7 per cent were born of primiparous mothers. It was found that 12.7 per cent of the illegitimate and 8.8 per cent of the legitimate newborn infants were immature.

In regard to weight, 2.7 per cent of the immature infants weighed less than 1 Kg.; 12.1 per cent, between 1 and 1.5 Kg.; 19.7 per cent, between 1.5 and 2 Kg., and 65.5 per cent, between 2 and 2.5 Kg.

The incidence of immaturity fell from 14.5 per cent of all births in the period from 1910 to 1918 to 8.1 per cent in that from 1928 to 1936. The death rate in the former period was 48 per cent and that in the latter, 20.5 per cent; 65 per cent of the deaths were in the first three days of life. All infants weighing under 1 Kg. died, and 92.3 per cent of all those weighing between 1 and 1.5 Kg. died. The mortality rate among illegitimate infants was approximately three times that among legitimate ones. The mortality rate of immature infants receiving mother's milk was 8.5 per cent; that of immature infants receiving some mother's milk, 12.5 per cent, and that of the artificially fed, 48 per cent.

HIGGINS, Boston.

NATURE OF SO-CALLED CONGENITAL WRYNECK: I. ITS CONSTITUTIONAL AND INHERITED PATHOLOGY. H. ABELS, Ann. pædiat. **152**:4 (Oct.) 1938.

Abels states that he and his colleagues have observed for many years that so-called congenital wryneck owes its direct origin (formal genesis) to an intrauterine postural deformity (Voelcker). He gives 3 observations in support:

1. There is a striking dependence of the side of development on certain positions of the fetus (immediate causation by external influence).

2. There is parallelism with other signs of asymmetry—in the external ear, the soft parts of the neck, the skull and the jaw. These signs can be observed in a moderate degree in the newborn more often than wryneck, but they always occur under the same circumstances which produce wryneck, e. g., breech presentation.

3. It can be shown at the time of birth that there is an atrophic state (pressure) of the sternomastoid muscle which only later leads to reactive formation of connective tissue.

FROM AUTHOR'S SUMMARY.

NATURE OF SO-CALLED CONGENITAL WRYNECK: II. ITS CONSTITUTIONAL AND INHERITED PATHOLOGIC ELEMENTS. H. ABELS, Ann. pædiat. **152**:96 (Nov.) 1938.

The opinion that so-called wryneck is a hereditary disease is repudiated by the localized histologic changes, by the facts presented as to its formal genesis (e. g., the role played by breech presentations) and finally by numerical incongruities. Extensive series of siblings with the condition point to a mechanical cause in the generative organs of the mothers. Abels' observations and repeated surgical experiences indicate an individually different reactibility of muscles previously damaged by intrauterine pressure. The occurrence in families of supranormal reactibility of a general nature could be demonstrated in the form of a simultaneous abnormal debility of the tissues, liability to edema and nephropathia; further, there was abnormal vulner-

ability of other mesoblastic descendants, e. g., severe degrees of asymmetry of the skull, either appearing combined with wryneck or, within one family, alternately with it. Likewise the occasional hereditary appearance of wryneck is explained by the occurrence in families of an increased reaction to the not at all rare effects of intrauterine pressure.

FROM AUTHOR'S SUMMARY.

ACCURACY OF THE "SIMILARITY DIAGNOSIS" (AEHNICHKEITSDIAGNOSE) IN TWIN RESEARCH. B. DUIS, Med. Klin. **35**:947 (July 14) 1939.

A "similarity diagnosis," which is based on a comparison of characteristics not readily influenced by environment, is considered much more accurate with respect to single and double ovum twins than is a diagnosis based on placental findings. The results of blood grouping and of other examinations of the blood are most important.

SIEMSEN, Chicago.

Newborn

BLOOD STUDIES ON THE NEWBORN: I. DETERMINATION OF HEMOGLOBIN VOLUME OF PACKED RED CELLS, RETICULOCYTES AND FRAGILITY OF THE ERYTHROCYTES OVER A NINE-DAY PERIOD. T. R. WAUGH, F. T. MERCHANT and G. B. MAUGHAN, Am. J. M. Sc. **198**:646 (Nov.) 1939.

The average total hemoglobin content of 100 cc. of the blood of newborn infants in Montreal, Canada, at birth is about 15.6 Gm. (100 per cent); it falls 0.66 Gm. (5 per cent of the original value) within the first nine days of life.

The average volume of packed red cells from newborn infants in this locality is 51.3 per cent (108 per cent of the figure for normal adults); it falls 5.4 per cent (10.5 per cent of the original value) in nine days.

As the decreases in hemoglobin and volume of packed red cells are not identical, it is apparent that the mean corpuscular hemoglobin concentration rises (from 30 to 32 per cent) during the first nine days, approaching the concentration found for the hemoglobin of adults in this region.

The average figures on hemoglobin and volume of packed red cells for infants in whom clinical icterus develops are only slightly lower than those for the non-icteric group. No correlation could be demonstrated between the original height or subsequent changes in individual values and the appearance of clinical jaundice.

Reticulocyte estimations are similar to those reported by other investigators.

The fragility of the erythrocytes in newborn infants as determined by the hemolytic index is normal at birth. The index falls, indicating a greater resistance, during the first four days, after which it returns toward normal.

The curves of erythrocyte fragility demonstrate a constant and characteristic degree of anisohemolysis throughout the period studied.

EMSKE, Omaha.

FACTORS ASSOCIATED WITH FETAL AND NEONATAL DEATHS. E. L. POTTER and F. L. ADAIR, J. A. M. A. **112**:1459 (April 22) 1939.

During a seven year period of about 18,000 births, there were 21 deaths per thousand live births and 23 stillbirths. Only 6 per cent of the babies were premature, but the mortality of the premature was eighteen times (35 per cent) that of full term babies. Many factors are correlated in this large statistical study, such as the relation of causes of death in different groups to maternal conditions and types of delivery.

Of the most important causes of death, anoxemia shows the highest incidence in babies delivered by version and extraction and by cesarian section; malformation, in natural cephalic deliveries and in those aided by low forceps, and intracranial hemorrhage, in high forceps extractions and breech deliveries. Anoxemia occurs

with equal frequency in full term and premature groups; malformations are twice as common in infants at term, and an exception to common belief was the finding that intracranial hemorrhage occurs as the cause of death twice as frequently in full term as in premature infants.

HEERSMA, Kalamazoo, Mich.

INTRACRANIAL HEMORRHAGE IN THE NEWBORN. M. H. ROBERTS, J. A. M. A. **113**:280 (July 22) 1939.

The records of 19,000 newborn infants were consulted as to the occurrence of intracranial hemorrhage at delivery; 10,000 of these were Negroes. All were checked after birth by repeated examinations, usually including spinal puncture. Intracranial hemorrhage was recorded in 132 cases, an incidence of 0.7 per cent. Of the patients, 77 died. If the condition could be recognized in all cases, the incidence would probably be between 1 and 2 per cent. When death occurred, it usually occurred within three days after birth.

Of the survivors, about 60 per cent were normal after several years' follow-up. In many instances spastic paralysis is probably due to maldevelopment of the brain.

HEERSMA, Kalamazoo, Mich.

EPIDEMIC DIARRHEA OF THE NEWBORN: A REPORT OF THREE OUTBREAKS. C. J. BAKER, J. Pediat. **14**:183 (Feb.) 1939.

Three epidemics of diarrhea which occurred among the newborn infants in the New York Hospital from 1935 to 1938 are reported. Fifty-nine full term infants were involved in the first epidemic, with a morbidity rate of 17.5 per cent; 13 premature infants, in the second epidemic, with a morbidity rate of 81 per cent, and 13 full term infants, in the last outbreak, with a morbidity rate of 6 per cent. No definite pathogenic organism was found in the stools of the full term infants. From the stools of 70 per cent of the premature infants cultures of Bacillus coli mutabile, Bacillus coli haemolyticus or both were obtained. The infants in the first and second epidemics were, for the most part, not clinically sick, and they responded to simple isolation and modifications of their feeding. The third group were all severely ill, and vigorous treatment was necessary, including starvation, parenteral injection of fluids, transfusions and careful resumption of feeding.

RAUH, Cincinnati.

HEMORRHAGIC DISEASE OF THE NEWBORN: A CRITICAL CONSIDERATION. S. H. CLIFFORD, J. Pediat. **14**:333 (March) 1939.

Clifford presents a critical review of the subject of hemorrhage in the newborn. In its original sense "hemorrhagic disease" referred to the syndrome of spontaneous external or internal hemorrhage occurring in the newborn, excluding that associated with trauma, accident or some definite disease. If this definition of the disease is used, comparable groups have been found to have a mortality rate between 30 and 38 per cent. The diagnosis of "hemorrhagic disease" can be made only on clinical grounds until its cause is established, in the absence of characteristic pathologic or consistent laboratory observations. An abnormal coagulation or bleeding time should not be a prerequisite for the diagnosis. Cases in which the hemorrhage is internal should not be automatically excluded on the presumption that the bleeding is of traumatic origin. The most important factor influencing the mortality in "hemorrhagic disease" is the point of origin of the bleeding. Cases in which there is external hemorrhage alone not only are encountered most frequently but have practically no mortality. Cases in which there is internal or internal and external hemorrhage have a mortality of 70 per cent at the Boston Lying-in Hospital. The impression that the present mortality in "hemorrhagic disease" is very low has arisen from the error in comparing subgroups obtained by classifying cases according to the location of the bleeding with undivided groups,

containing all cases. In comparable groups there has been no appreciable reduction in mortality from 1894 to the present, irrespective of the type of treatment or lack of treatment. In the treatment of severe anemia, irrespective of its cause, transfusion with whole blood is of value and often life saving.

RAUH, Cincinnati.

OSSEOUS DYSTROPHY FOLLOWING ICTERUS GRAVIS NEONATORUM. F. BRAID, Arch. Dis. Childhood. **14**:181 (Sept.) 1939.

Two infants had icterus gravis neonatorum, acholia, pathologic pigmentation of the skin and the same type of osseous dystrophy. One of the infants, a girl, showed precocious sexual development. Similar cases are cited from the literature. The report of a biopsy of bone taken from the older child is given. Evidence of dysfunction of the liver is presented, and the relation between hepatic dysfunction and bone dystrophy is discussed. Cirrhosis of the liver is known to be a sequel to icterus gravis neonatorum. It is argued that in these infants the bone dystrophy was the result of a failure of the liver to store and utilize vitamins and was therefore a sequel to icterus gravis neonatorum. No explanation can be considered complete, however, until the problem of the cause of icterus gravis has been solved.

KELLY, Milwaukee.

DUODENAL ULCERATION IN THE NEWBORN. W. HUNTER and H. W. DRYERRE, Brit. M. J. **2**:15 (July 1) 1939.

This is a report of what appears to be an unusual case.

ROYSTER, University, Va.

BREECH DELIVERIES, WITH SPECIAL REFERENCE TO THE PRIMIGRAVIDA. J. B. DEWAR, Tr. Edinburgh Obst. Soc., 1939, p. 125; in Edinburgh M. J., August 1939.

Dewar discusses breech delivery with reference to the primigravida and the fetal mortality in such deliveries. Asphyxia of the fetus, he states, is not the preeminent factor of danger; it is the fear of this by the obstetrician, which causes him to use too rapid and too forceful methods, resulting in injuries frequently fatal. Intracranial hemorrhages are known to be common and dangerous in these deliveries. Heidler reported them in 80 per cent of 99 infants born dead following breech delivery. Dewar discusses also other injuries to the fetus. He describes the technic which he has employed in a series of breech deliveries.

NEFF, Kansas City, Mo.

CASE OF KERNICTERUS. R. S. ILLINGWORTH, Proc. Roy. Soc. Med. **32**:1200 (Aug.) 1939.

The case reported concerned a girl of 11½ years.

WILLIAMSON, New Orleans.

THE INHERITED FORM OF ERYTHROBLASTOSIS IN NEWBORN INFANTS. H. D. PACHE, Ztschr. f. Kinderh. **61**:86 (June 6) 1939.

The frequency of familial incidence of the three forms of erythroblastosis of the newborn, hydrops foetalis universalis, icterus gravis neonatorum and erythroblastic anemia of the newborn, repeatedly raises the question of whether the condition is inherited.

In a previous paper the author presented evidence against such a conception, one of the strongest arguments being the greater incidence among children born later in the family. He states, however, that there is a small group of cases in

which the possibility that the disease is inherited cannot be denied and reports a case in support of this contention. The family tree in this case and the family trees in cases reported by other authors are presented and compared. In 6 of the 10 cases reported by the author recovery followed repeated transfusions.

SIEMSEN, Chicago.

ANAEMIA NEONATORUM. S. D. KIRIMLIDIS, Ztschr. f. Kinderh. **61**:111 (June 6) 1939.

Icterus gravis, hydrops universalis and anaemia neonatorum form a triad of primary idiopathic congenital anemias. The term "fetal erythroblastosis" is not entirely correct, because erythroblastosis may be absent.

Anaemia neonatorum is present at the time of birth or appears within the first two weeks of life, usually about the end of the first week. It is differentiated from secondary anemia by the absence of hemorrhage or illness which might cause anemia. There are two types: (1) erythroblastic or regenerative and (2) aplastic. The latter type is more common. Clinically, marked pallor with a good general condition is characteristic.

The author discusses the causes, the blood picture, the diagnosis, the mortality and the therapy of anaemia neonatorum and reports 2 cases. Both patients recovered following transfusions and liver therapy. Even patients in whom the condition is severe may recover without any therapy.

SIEMSEN, Chicago.

Acute Contagious Diseases

SEQUELAE OF POSTMEASLES ENCEPHALOMYELITIS. N. MALAMUD, Arch. Neurol. & Psychiat. **41**:943 (May) 1939.

Malamud reports 2 cases of postmeasles encephalomyelitis, listing the usual clinical and pathoanatomic sequelae.

BEVERLY, Chicago.

SCARLET FEVER OUTBREAK TRACED TO RAW MILK. Health News **16**:204 (Dec. 11) 1939.

In 18 cases of scarlet fever in Hornell, N. Y., the infection was traced to raw milk. An employee of the dairy was found to have a sore throat, and a culture of material from his throat was positive for hemolytic streptococci. Also, one of the cows had a diseased udder.

AIKMAN, Rochester, N. Y.

INTRAVENOUS TREATMENT OF MENINGOCOCCIC MENINGITIS WITH MENINGOCOCCUS ANTITOXIN. A. L. HOYNE, J. A. M. A. **107**:478 (Aug. 15) 1936.

The average mortality rate among patients with meningococcic meningitis during the nineteen years before 1934 at the Cook County Hospital, Chicago, was 50.6 per cent. The underlying condition is considered an infection of the blood stream accompanied by toxemia, and meningitis is considered a complication. Intrathecal therapy prolongs the recovery of the patient. Intravenous injection of massive doses of the therapeutic agent is advised. Sixty patients receiving only intravenous therapy had a mortality rate of 11.8 per cent, and 43 patients of 20 years or less, a rate of 2.3 per cent. Among the patients treated by the intravenous route exclusively, the fatality rate was 15.9 per cent. Of 9 meningococcic patients treated intravenously without any lumbar puncture, only 1 died. Suppurative complications are not encountered with intravenous therapy. Fewer complications were found after the use of Ferry's meningococcus antitoxin than after the use of other serums.

BONAR, Salt Lake City.

THE EARLY TREATMENT OF POLIOMYELITIS AND THE IMPORTANCE OF PHYSICAL THERAPY. A. T. LEGG, J. A. M. A. **107**:634 (Aug. 29) 1936.

The recent outbreak of poliomyelitis brings to mind again the need to emphasize the importance of good after-care. A long period of competent follow-up treatment will prevent deformities and favor the regaining of muscle power. Complete rest and immobilization of the limbs should be insisted on as soon as the paralysis or weakness appears. This will prevent contracture and help relieve the pain in the sensitive stage. As soon as the sensitive stage is over, a complete examination of the muscles should be made and a course of muscle training planned. A check-up of the gain or loss of muscle power should be made at definite intervals for years. Graphs show that the greatest gain occurs in the first year but that continued treatment aids in real progress over a long period of time.

BONAR, Salt Lake City.

A CONTROLLED STUDY OF PERTUSSIS PROPHYLAXIS: A COMPARISON OF PHASE I, H. PERTUSSIS VACCINE WITH UNDENATURED BACTERIAL ANTIGEN. C. H. SINGER-BROOKS, J. Pediat. **14**:25 (Jan.) 1939.

During a three year period observations were made on: (1) 95 children given injections of undenatured bacterial antigen; (2) 272 children given injections of phase I Haemophilus pertussis vaccine, and (3) 256 children used as controls. Of the 95 children treated with undenatured bacterial antigen, 34 were exposed and 28 (or 83.3 per cent) contracted pertussis. Six (17.6 per cent) of the exposed children escaped attack. The rate of attack among the total of 95 children was 29.4 per cent. Of the 272 children treated with phase I H. pertussis vaccine, 42 were exposed to pertussis; of these, 7 (16.6 per cent) contracted pertussis, while 35 (83.4 per cent) of the exposed children escaped. The rate of attack in the total group of 272 children was 2.5 per cent. Of the 256 children used as controls 71 were exposed to pertussis, and 62 (87.2 per cent) of these contracted the disease. Nine (12.6 per cent) of the exposed children escaped. The rate of attack for this group was 24.2 per cent.

RAUH, Cincinnati.

PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES. Pub. Health Rep. **54**:1587 (Sept. 1) 1939.

The incidence of poliomyelitis during the period from July 16 to Aug. 12, 1939 was 783 cases, an incidence higher than the previous year's but not higher than the current incidence. There were 208 cases in the Pacific Coast region, 214 in the East North Central region (including Michigan), and there was an increase in South Carolina. Other sections of the country reported lower figures than those. The incidence of influenza was 10 per cent above median. The numbers of cases of diphtheria, measles, meningitis, scarlet fever, smallpox and typhoid fever were below the seasonal incidence. The average mortality rate for large cities was 9.7 per thousand population, the lowest since 1932, when the rate was the same.

SANFORD, Chicago.

A CRITICAL CONSIDERATION OF SOME OF THE IMMUNOLOGICAL PROBLEMS WITH SPECIAL REFERENCE TO DIPHTHERIA. R. A. Q. O'MEARA, Irish J. M. Sc., November 1939, p. 778.

O'Meara discusses the problem of diphtheria. He believes that the purification of diphtheria antitoxin has reached a point where it has lowered the toxin-combating properties of the serum so far as treatment of the disease in man is concerned. He also states that the same may be said for many of the prophylactic measures used in artificial production of active immunity.

SNELLING, Toronto, Canada.

THE MANZULLO TEST IN THE DIAGNOSIS OF DIPHTHERIA. J. G. TYMAN, Irish J. M. Sc., November 1939, p. 790.

The Manzullo test is made by painting a 2 per cent solution of potassium tellurite on the exudate, which is previously white; the exudate darkens within fifteen minutes if it is due to diphtheria, but not if it is due to infection with other organisms, including Vincent's. Tyman tried out the test in 75 unselected cases. The test was positive in 38 cases of diphtheria, clinically and bacteriologically demonstrated, and negative in 5 cases of diphtheria. It was also positive in 10 cases of conditions other than diphtheria. The author feels that the test is not reliable.

SNELLING, Toronto, Canada.

IMMUNIZATION OF TUBERCULOUS CHILDREN IN THE HOSPITAL AT BRÉVANNES, WITH MIXED ANATOXIN (DIPHTHERITIC AND TETANIC). M. CHEVALLEY and P. G. ZIVY, Bull. Soc. pédiat. de Paris **37**:26 (Jan.) 1939.

This immunization of tuberculous children in an institution which admitted 1,800 children over a period of three and a half years resulted in the disappearance of diphtheria. Three doses of 2 cc. each of mixed diphtheria and tetanus anatoxin were injected at intervals of three weeks. One hundred and seventy-six children were observed with regard to reactions. Eighty-six per cent of the children under 4 years of age with primary tuberculous lesions had febrile reactions; 42 per cent of those between 4 and 7 years old and 43 per cent of those from 7 to 15 years old showed similar reactions. In two thirds of the patients the fever was mild and constituted the only manifestation of reaction. In one fifth of the patients the fever was associated with infection of the upper respiratory tract, and 6 patients who were closely associated with one another had digestive disturbance and apparently catarrhal jaundice. No instance of reactivation of a tuberculous focus occurred after the injection of anatoxin.

BENJAMIN, Montreal, Canada.

HAPPENINGS IN THE TRACHEA OF GUINEA PIGS AFTER INTRATRACHEAL APPLICATION OF DIPHTHERIA BACILLI. E. REISS, Arch. f. Hyg. **123**:49 (Oct. 15) 1939.

The effects exerted on the tracheal mucous membranes of guinea pigs by a strain of diphtheria bacilli (Di-bacilli) producing a weak toxin and another one producing a strong toxin have been investigated histologically.

Under general anesthesia, after intramuscular injection of a 20 per cent solution of ethyl carbamate (urethane) (0.7 Gm. per kilogram), as suspension of the bacilli was injected into the trachea through a very fine needle. The animals were killed one at a time after ½, 4, 7, 16, 24, 48, 72, 96 and 144 hours. After fixation in a solution of formaldehyde and embedding in paraffin, the trachea was investigated in longitudinal serial sections, stained with Gram's stain.

Both these strains became phagocytosed alike by leukocytes in the lumen of the trachea without having invaded the mucous membranes. The phagocytosis started after half an hour and was finished after about forty-eight hours. While apathogenic bacteria (staphylococci, hay bacilli and sarcinas) became phagocytosed quickly, especially with the aid of the epithelial cells, pathogenic bacteria invaded mucous membranes without being phagocytosed. The Di-bacilli held a somewhat intermediate position in their pathogenicity for guinea pigs.

While the strongly toxic Di-bacilli were removed in the same manner and time as the bacilli of little toxicity, animals treated with the strongly toxic strain died, even when the bacilli had been removed from the mucous membranes a long time before.

Reiss assumes, therefore, that the antigens of the weakly toxic bacilli differ in their nature from those of the strongly toxic ones. This fact should be considered in testing for antibodies.

FALKENHEIM, Rochester, N. Y.

PERTUSSIS AND THE SEDIMENTATION RATE OF RED BLOOD CELLS. A. CHATTÁS, Kinderärztl. Praxis **7**:345 (Aug.) 1936.

Chattás found that the sedimentation rates of children who had uncomplicated whooping cough were slightly increased as compared, according to age groups, with the values obtained for healthy infants and children. He states that normal values were rarely and diminished values were never obtained, having in mind that growing infants normally show low values. HEYMANN, Cleveland.

THE COLOGNE EPIDEMIC OF POLIOMYELITIS AMONG ADULTS DURING THE FALL OF 1938. M. FEY, Med. Klin. **35**:538 (April 21) 1939.

Of 371 patients, 64 were adults. The epidemic started later among adults than among children. The morbidity and mortality were greater among males. The findings in the spinal fluid did not parallel the severity of the disease; an increase in cells and in protein was not always present. The clinical course afforded no information regarding subsequent paralysis. No serum was given. Paralysis developed in about 50 per cent of the patients. STEINSEN, Chicago.

TREATMENT OF DIPHTHERIA BACILLUS CARRIERS WITH VITAMIN A AND DETOXIN. A. KLINZING, München. med. Wchnschr. **86**:1267 (Aug. 18) 1939.

A group of carriers of diphtheria bacilli in whom the usual methods of treatment, carried out for three or four weeks, had no effect were given vitamin A. No beneficial result from the administration of the vitamin could be observed. Eighteen children received 5 cc. of detoxin intramuscularly on alternate days until three doses had been administered. Four children gave negative cultures after the first dose and 5 others after three doses. Of those who failed to respond, 2 came from the same village and 4 from the same hospital, where they had contracted nasal diphtheria. Klinzing believes that success or failure with detoxin depends on the strain of bacillus present. BRAHDY, Mount Vernon, N. Y.

PREVENTION OF SCARLET FEVER AND DIPHTHERIA IN VIENNA. O. VON KOPETZKY, Wien. klin. Wchnschr. **51**:555 (May 20) 1938.

Von Kopetzky brings out several interesting points in regard to the prevention of scarlet fever and diphtheria in Vienna. He notes that the practice of keeping home from school not only the child afflicted with either disease but also the children sitting nearby, because they had been exposed to the disease, proved efficacious in preventing the spread of these infections.

In an early statistical summary it was noted that the age group from 4 to 6 years had the greatest percentage of patients suffering from diphtheria. Statistics for 1933-1935 reveal that the group aged 7 and 8 years had the highest percentage, indicating that the opportunities for infection are more common at school than at home.

The author points out that carriers are an important source of infection and that probably 1 per cent of the total population are carriers.

He also notes that a great percentage of children with active scarlet fever and diphtheria are hospitalized in Vienna. Reinfection during convalescence was less frequent in patients discharged from hospitals in which newly admitted patients were not permitted to come in contact with convalescent ones. Patients convalescent from scarlet fever when discharged from the hospital are further quarantined at home for ten days.

The author wisely points out that in the future the prophylaxis of scarlet fever and diphtheria will lie in active immunization. ABT, Chicago.

SUBCUTANEOUS VACCINATION BY THE FRACTIONAL METHOD. H. HOSOI, Acta pædiat. japon. **45**:786 (June) 1939.

According to the experience gained by Hosoi with the fractional method of subcutaneous vaccination, the systemic reaction following inoculation of the first fractional dose (1/6 to 1/60) was minimal. After inoculation of the remaining fraction of the dose, 20 to 36.5 per cent of the subjects showed a positive reaction. Repeating the experiment on rabbits, he found that the detoxicating titer against the smallpox virus increased proportionately with the duration of the intervals between the first and second inoculations.

KATO, Chicago.

VACCINATION AGAINST SMALLPOX. B. P. B. PLANTENGA, Maandschr. v. kindergeneesk. **5**:450 (Aug.) 1936.

Plantenga gives the history of vaccination and its consequences, especially encephalitis. He discusses the means of preventing postvaccinal encephalitis, in the occurrence of which a hereditary influence is undeniable. The child with an inferior nervous system should not be vaccinated, nor the children with a skin disease or a disturbance in metabolism. He discusses the occurrence of encephalitis in consequence of infectious diseases such as measles and whooping cough. He strongly recommends vaccination of children below the age of 1 year.

VAN CREVELD, Amsterdam, Netherlands.

ENCEPHALOMYELITIS POSTVACCINALIS. B. BROUWER, Maandschr. v. kindergeneesk. **8**:379 (July) 1939.

The number of cases of postvaccinal encephalomyelitis in the Netherlands has been diminishing in recent years because the frequency of vaccination has decreased. In 1927 there were still 150,653 vaccinations; in 1938, only 20,833. In 1937 there were 6 cases and in 1938 3 cases of encephalomyelitis which were accepted by the Governmental Committee for Encephalitis as postvaccinal in origin. In 2 of these the condition was studied histologically. Typical areas of demyelinization with perivascular increase of microglia cells were found scattreed through the entire central nervous system. However, the meninges failed to show distinct reaction. The histologic picture was compared with that found in a case of myeloencephalitis following variola. It was also compared with that in a case clinically resembling one of postvaccinal encephalitis. The histologic appearance in this case, however, was different. The author does not accept the theory of activation of a virus already present in the central nervous system before vaccination. He believes that the encephalitis is caused by the vaccinia virus itself but that an endogenous factor must also be considered.

VAN CREVELD, Amsterdam, Netherlands.

THE DIFFERENT TYPES OF DIPHTHERIA BACILLI AND THE CLINIC FOR DIPHTHERIA IN THE NETHERLANDS. W. A. TIMMERMAN, A. C. BRANDWYK and E. A. J. PEL, Nederl. tijdschr. v. geneesk. **80**:3546 (Aug. 1) 1936.

In Holland the types of the diphtheria bacilli cultivated from the throat schwabs of 370 patients with diphtheria have been determined. The great majority of the strains could be identified as belonging to one or the other of Anderson's three types, only a small fraction showing anomalies. Although those belonging to the gravis type preponderated, the diphtheria clinically was very benign, not presenting a severer course than the mitis infections. The mortality showed no difference. Myocarditis occurred as well in the mitis as in the gravis infections. Postdiphtheritic pareses and albuminuria did not occur in the patients with mitis infections. Even under the very mild endemic conditions now prevailing in the Netherlands, early serum treatment is indicated.

VAN CREVELD, Amsterdam, Netherlands.

Acute Infectious Diseases

OBSERVATIONS ON THE SPECIFIC TREATMENT (TYPE A ANTISERUM) OF STAPHYLOCOCCAL SEPTICEMIA. L. A. JULIANELLE, Ann. Int. Med. **13**:308 (Aug.) 1939.

The preparation and administration of the type A antiserum are described.

Seventeen patients with staphylococcic septicemia recovered after the use of this antiserum. Ten patients who received the antiserum died.

READING, Galveston, Texas.

NOTES ON MALARIA IN CHILDREN. M. W. BEACH and G. D. JOHNSON, Arch. Pediat. **56**:639 (Oct.) 1939.

The patients studied were hospitalized between the years 1928 and 1937. There were 262 children, aged between 4 months and 12 years; 113 were white children and 149 were Negroes; 146 were males and 116 were females.

October is the month during which the most children with malaria are admitted. Rainfall, hours of sunshine and temperature apparently have no effect on the incidence. The incidence is greatest in children between 2 and 8 years of age.

The tertian form was most commonly the causative organism, with the estivoautumnal form next.

Fever was present in 91.2 per cent of the patients; chills, in 27.8 per cent. The spleen was palpable in 50 per cent of the patients on admission.

Among the children whose condition was uncomplicated, 80 per cent had a white cell count below 10,000 on admission; only 14 had a count of over 12,000, and these were all under 2 years of age and had cerebral involvement or a mixed (estivoautumnal and tertian) infection.

The diagnosis was made in 75 per cent of all cases during the first two days of hospitalization. Organisms were never found in 18 cases.

Fifteen patients, or 5.76 per cent of those admitted, died. All but a single child died within the first forty-eight hours.

Treatment consisted in the use of quinine or atabrine or various combinations of these two with plasmochin. These drugs were all equally effective in relieving symptoms. No ill effects followed the use of any of the drugs. ORR, Buffalo.

OCCURRENCE OF THE DIFFERENT GROUPS OF HEMOLYTIC STREPTOCOCCI IN HUMAN INFECTIONS. H. M. GARDNER, Edinburgh M. J. **46**:648 (Oct.) 1939.

Gardner gives the sources of her material as throat and nose swabbings from patients in various hospitals, including the Royal Hospital for Sick Children. There is a short description of the preparation of the immune serums, of the isolation of strains and preparation of extracts and of the results of precipitin tests.

Group A plays the dominant role in human infection (79.9 per cent of the strains). Group B, C and G were obtained from various diseases, including tonsillitis; group G came from tonsillitis and scarlatina. There were three strains of group H from scarlatina and otitis media. NEFF, Kansas City, Mo.

MALARIA TRANSMITTED BY INJECTION OF BLOOD IN TWO INFANTS AGED SIX AND NINE MONTHS. E. HURMUZACHE, Bull. Soc. de pédiat. de Iasi **9**:21, 1938.

Symptoms of malaria developed in 2 infants ten and twenty-five days, respectively, after injections of blood from apparently healthy donors. Organisms similar to those found in the infants were found later in smears of blood from the donors.

LESLIE, Evanston, Ill.

SIMPLE DISLOCATION OF THE HIP IN THE COURSE OF PNEUMOCOCCEMIA. C. NAZZARO, Pediatria **47**:422 (May) 1939.

Nazzaro describes the case of a 5 year old child with bronchopneumonia complicated by purulent otitis media and suppuration of the right knee. From the pus a pneumococcus was cultured. There was marked contraction of the lower extremities, so that any attempt at extension caused marked pain. Dislocation of the right hip was confirmed by roentgenogram. The author considers three possible causes of the dislocation: relaxation of the capsule of the joint, muscular contraction and the abnormal position of the child in bed.

MARTOCCIO, Utica, N. Y.

PATHOLOGY AND EPIDEMIOLOGY OF INFANTILE SALMONELLOSIS. E. HORMAECHE, Arch. de pediat. d. Uruguay **10**:445 (Aug.) 1939.

Hormaeche has studied 200 cases of infantile salmonellosis. All of the infections were of animal origin. The symptoms of enteritis set in very abruptly. In the young child the infection often begins with angina and rhinopharyngitis. Otitis may also be associated as a complication, and occasionally meningitis. Occasionally the patients have only moderate diarrhea and present only simple dyspepsia, or they may not have any intestinal manifestations. In many the illness is quite protracted. Septicemia, cystitis and pyelonephritis are often complications.

The disease can occur in the breast-fed infant and in the infant fed on sterilized foods. It occurs usually in children of large families. Older children and adults may escape the infection. The author believes that infants have less resistance to the infectious agent than have adults. This infection should always be searched for in chronic forms of enteritis, whether enteral or parenteral in origin.

SCHLUTZ, Chicago.

HYPERSENSITIVENESS IN ACUTE INFECTIOUS DISEASES. H. P. SECKEL, Ann. pædiat. **152**:73 (Nov.) 1938.

A series of criteria for recognizing hypersensitiveness as a pathogenic factor in acute infectious diseases are enumerated. Under the guidance of these criteria the clinical, epidemiologic and pathologic facts suggestive of hypersensitivity of infection are brought together in relation to such diseases as rheumatic fever, scarlet fever and lobar pneumonia. Seckel's hypothesis of toxic diphtheria as representing a hypersensitivity reaction to products of the diphtheria bacillus is discussed in a similar way. As there are reactions to the same bacteria in which there is nothing to suggest hypersensitiveness to infection, a corresponding group of diseases may be differentiated as nonhyperergic or hypoergic acute infectious diseases.

FROM AUTHOR'S SUMMARY.

LYMPHOCYTIC FEVER. S. ROSENBAUM, Ann. pædiat. **152**:117 (Nov.) 1938.

Observations are reported on 59 children aged chiefly up to 2 years who became ill in the manner of an endemic with undulating fever, slight swelling of the glands, enlargement of the liver and spleen, marked lymphocytosis with monocytoid plasma cells and pallor. The illness lasted months and sometimes more than a year. The issue was always favorable. The were no home or family infections. The illness had its start chiefly in the period from May to September. Frequent complications were tonsillitis and otitis media; at the time of complications there was sometimes polynucleosis instead of lymphocytosis. The Hanganatziu-Deicher reaction was negative. There was no identity with Pfeiffer's glandular fever or with lymphocytic angina. It is supposed that this is a specific illness, perhaps transmitted by insect bites.

FROM AUTHOR'S SUMMARY.

IMMUNITY IN HUMAN INFANTS. K. HELLER, Ann. pædiat. **152**:210 (Jan.) 1939.

Ehrlich discovered the immunization of mice through suckling. This phenomenon was further demonstrated in various other mammals. Among the investigations in man up to the present date those reported by Groër and Kassowitz fail to furnish direct proof. The experiments of Salge, Much and Happich demonstrated a passing of antitoxins into the baby by way of the milk, but when these results were checked it was found that this occurrence is not so frequent or so intense that it could be of much biologic importance. The different reactions to infection observed in breast-fed and bottle-fed children cannot be explained by immunity of a trophogenic origin.

FROM AUTHOR'S SUMMARY.

TYPHOID FEVER IN CHILDREN WITH MANIFESTATIONS PREDOMINANTLY CATALEPTIC. J. B. NICOPOULOS, Ann. pædiat. **154**:286 (Feb.) 1940.

Two cases are reported of typhoid with grave complications, such as absence of facial movement, suppression of kinetic initiative, waxen flexibility of the limbs, cataleptic postures, torpor and abnormal reflexes. The complete cure points to a toxic influence on the nervous system which produced the picture of typhoid encephalitis.

FROM AUTHOR'S SUMMARY.

SEPSIS IN CHILDHOOD. A. FYOW, Monatschr. f. Kinderh. **80**:42, 1939.

In this 60 page article Fykow reports cases and lists the types of general sepsis resulting from local sepsis encountered in his practice. There is nothing of particular interest to American pediatricians in this survey. He records cases and discusses sepsis arising from the intestine, the navel, the mouth, tonsils and pharynx, the ears, the skin and the bones, as well as sepsis from the cardiovascular system, e. g., subacute bacterial endocarditis; he also discusses sepsis arising from the urinary system and last but not least that of unknown origin. The reviewer gets the impression that the lot of Bulgarian children is not a happy one. Most readers will agree with the author that the treatment is not especially simple and that supportive measures are indicated. He thinks that local foci of infection should be removed.

GERSTLEY, Chicago.

ROLE OF NERVOUS STIMULATION IN THE DEVELOPMENT OF RABIES. I. A. PIGALEV, Arkh. biol. naouk **53**:52, 1939.

This experimental study was undertaken to ascertain the role played by stimulation of the peripheral nerves in the development of various trophic disturbances, not only in the region of stimulation but also in the brain. For this purpose, from 0.2 to 0.3 cc. of dilute solution of formaldehyde U. S. P. (1:50) was injected into the exposed left sciatic nerve of a rabbit. The nerve was then sectioned, the central stump sutured to the muscle and the wound ligated. Immediately thereafter, 0.3 cc. of a 2 per cent emulsion of the virus fixé (rabies) was injected into the subarachnoid space. The rabbit was killed on the third day, before the development of symptoms of rabies. Pieces were then excised from the cortex of each cerebral hemisphere and 2 per cent emulsions prepared from this material. These emulsions were later injected into the subarachnoid space of normal rabbits. The rabbits given injections of the emulsions prepared from the left cortex were affected with rabies, while those given injections of the material from the right cortex remained immune or had an incubation period of from six to twelve days instead of the usual four days.

In another series of experiments, tetanus toxin was injected into the limb of a rabbit in a dose sufficient to produce local tetanus on the third day. At the same time the virus fixé (rabies) was injected into the subarachnoid space. The animal was killed on the third day, and emulsions were prepared from the pieces obtained from the cortex of each hemisphere. The emulsions were injected into

normal rabbits. It was found that rabbits receiving injections of the emulsion prepared from the ipsilateral cortex succumbed to rabies, whereas those treated with emulsion from the contralateral cortex were either immune or showed a prolonged period of incubation.

Pigalev draws the conclusion that stimulation at the peripheral end produces changes in the cerebral cortex and that a biologic stimulus, the virus fixé injected into the subarachnoid space, meets with different conditions in the two hemispheres, conditions which will determine the further reactions. According to Pigalev, this is the reason for the dissimilarity in the virus content and virulence of the cortex of the two hemispheres of the same animal. While one hemisphere may be entirely free of the virus, the other has sufficient to release all the symptoms of the disease. Pigalev claims that the virus itself undergoes biologic changes under the influence of the peripheral stimulation, as witnessed by the lengthening of the incubation period.

NOTKIN, Poughkeepsie, N. Y. [ARCH. NEUROL. & PSYCHIAT.]

Chronic Infectious Diseases

PRENATAL SYPHILIS IN ONE OF TWINS. U. J. WILE and D. G. WELTON, Am. J. Syph., Gonor. & Ven. Dis. **22**:544 (Sept.) 1938.

Wile and Welton review the literature on this subject in some detail, citing a report on syphilis in 1 of fraternal twins and also reports on syphilis in 1 of identical twins. They report on congenital syphilis in one of fraternal twins, both males.

ROYSTER, University, Va.

ACQUIRED SYPHILIS OF INFANCY AND CHILDHOOD: REPORT OF THIRTY-FIVE CASES. J. R. WAUGH, Am. J. Syph., Gonor. & Ven. Dis. **22**:607 (Sept.) 1938.

In 13 of the 35 cases of acquired syphilis of infancy and childhood the disease was acquired by sexual contact. The author does not explain how it was acquired in the other cases. His own summary of his article follows:

"There are presented the case histories of 35 infants and children with acquired syphilis.

"Of 24 infants and young children (22 of them from 5 months to 10 years of age, and 2 of them 11 years of age), only 2 acquired syphilis through definite sexual contact and 1 probably through sexual contact. The other 21 infants and children undoubtedly acquired syphilis from a parent, or a brother or sister. Of these 88 per cent were white and 12 per cent colored. The males and females were evenly divided. Only 4 children had a history of a chancre or a chancre present on admission. All 5 children in one family had acquired syphilis; there were 2 with acquired syphilis in another family. All of the families were indigents.

"There were 11 older children from 12 to 14 years of age who acquired syphilis definitely through sexual intercourse. Ten of them were sexual delinquents."

ROYSTER, University, Va.

ACQUIRED SYPHILIS IN CHILDREN: AN EPIDEMIOLOGIC AND CLINICAL STUDY. F. R. SMITH JR., Am. J. Syph., Gonor. & Ven. Dis. **23**:165 (March) 1939.

This is an exhaustive statistical study of cases gathered from a large number of clinics and from other authentic sources. There are several diseases, mostly in Europe and the Orient, which may closely resemble acquired syphilis and may be confused with it.

A study was made of 125 children under 10 years of age with primary syphilis. All the cases were authenticated at reputable institutions.

The disease was acquired in the following manner: (1) attempted sexual intercourse, 43; (2) kissing, 15; (3) household contact, 14; (4) transfusion, 9; (5) unknown (no date), 44.

The clinical manifestations do not differ materially from those in the adult. "The discovery of nine cases of transfusion syphilis in children emphasizes the necessity for the careful pretransfusion examination of all donors, including parents and relatives."

ROYSTER, University, Va.

VITAMINE A CONTENT OF HUMAN LIVER IN TUBERCULOSIS. P. D. CRIMM and D. M. SHORT, Ann. Int. Med. **13**:61 (July) 1939.

An average of 342 units (U. S. P.) of vitamin A per gram was present in the livers of 50 patients with tuberculosis. In 14 per cent of the livers the vitamin A content approached depletion. The administration of vitamin A is recommended for tuberculosis with pyrexia or enteritis.

READING, Galveston, Texas.

VALUE AND SIGNIFICANCE OF THE TUBERCULIN TEST. A. J. LOGIE, Ann. Int. Med. **13**:255 (Aug.) 1939.

The need for a more widespread use of the tuberculin test is stressed.

READING, Galveston, Texas.

THE USE OF SULFANILAMIDE IN PULMONARY TUBERCULOSIS; PRELIMINARY REPORT. E. B. FREILICH, G. C. COE and N. A. WIEN, Ann. Int. Med. **13**:1042 (Dec.) 1939.

Orally administered sulfanilamide was of no apparent value in altering the course of pulmonary tuberculosis.

READING, Galveston, Texas.

EARLY ACUTE ARSENICAL ERYTHEMAS: A STUDY OF ELEVEN CASES OF THE "ERYTHEMA OF THE NINTH DAY" OF MILIAN. O. CAÑIZARES and E. W. THOMAS, Arch. Dermat. & Syph. **39**:867 (May) 1939.

A study of 11 cases of "erythema of the ninth day" is reported. The early acute arsenical erythema presents sufficient distinctive features to be regarded as a clinical entity and should be differentiated from the later edematous exfoliative dermatitis. To the syphilologist, the practical importance of recognizing this entity lies in the safety of continuing arsenical therapy. The authors state that it seems advisable to stop treatment with arsenic during the early erythema and not to resume it until all signs of the reaction have disappeared. When the arsenical therapy is again instituted, the dose should be reduced and increased according to the patient's tolerance.

JACKSON, Iowa City.

ACETARSONE THERAPY IN ONE HUNDRED AND EIGHTY-SEVEN CASES OF CONGENITAL SYPHILIS, WITH OBSERVATIONS ON A GROUP OF EIGHTY-SEVEN PATIENTS RECEIVING NO TREATMENT. D. M. PILLSBURY and H. H. PERLMAN, Arch. Dermat. & Syph. **39**:969 (June) 1939.

From the literature the authors summarize the disadvantages and advantages of acetarsone in the treatment of congenital syphilis and report their experiences with the drug in the treatment of 187 patients with congenital syphilis. They conclude that the effect of acetarsone in arresting congenital syphilis is inferior to that of arsphenamine and bismuth preparations. The incidence of reactions is high; acetarsone cannot be controlled by experimental studies of spirocheticidal action and toxicity in animals, and administration to outpatients is not assured.

JACKSON, Iowa City.

VACCINATION AGAINST TUBERCULOSIS. H. M. KINGHORN and M. DWORSKI, New York State J. Med. **39**:810 (April 15) 1939.

Kinghorn and Dworski have worked at Saranac Lake, N. Y., for twelve years on caseous vaccine. The vaccine is made from caseous material from the lungs and lymph nodes of cattle having tuberculosis. The material is thoroughly dried, then ground in a mortar and in a porcelain ball mill for at least two weeks for eight hours daily. The process of manufacturing is described. The final product is sterilized, and sterility tests are made for tubercle bacilli and secondary organisms. In rabbits the caseous vaccine gives practically the same protection as does BCG; 89 per cent complete protection and 11 per cent minimal tuberculosis is shown, compared with 78 per cent complete protection and 22 per cent minimal tuberculosis for BCG. No advanced tuberculosis was shown after the use of either vaccine. BCG gave slightly longer immunity, and Kinghorn and Dworski consider it a "safe and a good vaccine."

"Reliance should not be placed solely on any vaccine to prevent or cure tuberculosis, and if vaccines are used, the usual preventive and curative measures should be faithfully employed. Caseous vaccine and BCG have a real value in tending to prevent tuberculosis."

AIKMAN, Rochester, N. Y.

TUBERCULOSIS OF THE LUNGS IN CHILDREN. C. MCNEIL, Tr. Med.-Chir. Soc. Edinburgh, 1939, p. 145; in Edinburgh M. J., October 1939.

Children were shown to illustrate three stages of tuberculosis: The primary focus, the focal extension of the primary focus and the general spread. They had all been hospitalized. One boy of 11 years had recovered from tuberculous pleurisy of several months' duration. A boy of about 3 years had shown a large area of consolidation in the upper lobe of the left lung but at the time of writing was a "standard specimen of a healthy child." A third boy, aged 11, who had shown chronic miliary tuberculosis was presented as a rare illustration of apparent, if only temporary, cure.

NEFF, Kansas City, Mo.

ERYTHEMA NODOSUM AND PHLYCTENULAR KERATITIS. R. PIERRET, A. BRETON and G. LEFEBVRE, Paris méd. **1**:255 (March 25) 1939.

The authors cite instances in which erythema nodosum or phlyctenular keratitis has recurred in a subject known to have had tuberculosis. They believe that in most instances such recurrences indicate a lighting up of an old infection or a reinfection, and that the patient should immediately receive thorough examination and study.

LESLIE, Evanston, Ill.

PSEUDOLEUKEMIC SYPHILITIC ANEMIA IN THE FIRST HALF-YEAR OF LIFE (SECONDARY ERYTHROBLASTOMA). A. R. GUERRA and E. PELUFFO, Arch. de pediat. d. Uruguay **10**:335 (June) 1939.

Pseudoleukemic anemia occurred in 4 children affected with virulent congenital syphilis, in the first half-year of life. Two of the patients showed icterus. One showed the symptom complex of early icteric anemia, often described under the title of idiopathic erythroblastosis of the newborn.

The authors believe that in the population of Uruguay other types of congenital infection which might cause similar types of anemia are the exception and that syphilis is usually a principal etiologic factor in splenic pseudoleukemia occurring in the first half-year of life.

SCHLUTZ, Chicago.

PULMONARY PROCESSES IN INFANTS WITH CONGENITAL SYPHILIS. J. R. MARCOS and S. MENDIVIL, Arch. de pediat. d. Uruguay **10**:463 (Aug.) 1939.

Five cases of congenital syphilis in which there were chronic pulmonary disorders are reported. The authors were of the impression that the pulmonary

changes were related in some way to the syphilitic taint in the patients. In no case was there a diagnosis of tuberculosis.

Antisyphilitic treatment produced rather striking and rapid improvement in the pulmonary conditions and also in the general state of health of the subjects.

SCHLUTZ, Chicago.

Diseases of Blood, Heart and Blood Vessels and Spleen

THE APPEARANCE OF THE T WAVE IN LEAD IV IN NORMAL CHILDREN AND IN CHILDREN WITH RHEUMATIC HEART DISEASE. M. ROBINOW, L. N. KATZ and A. BOHNING, Am. Heart J. **12**:88 (July) 1936.

Whereas 98 per cent of normal adults showed an inverted T wave in lead IV, this occurred in only 42 per cent of normal children. In the others, the wave was upright, diphasic or polyphasic.

The contour of the T wave in lead 4 in normal children may show considerable variation when electrocardiograms are taken a few months apart.

Children with active rheumatic heart disease show a higher percentage of upright T waves in lead IV than do normal children of the same age. The T wave tends to become inverted when recovery from the acute stage sets in and to become more upright when the disease process becomes aggravated. There are, however, exceptions to these correlations, and the authors conclude that the practical value of lead IV in children suffering from rheumatic heart disease is definitely limited.

The factors accounting for the differences in the T wave of lead IV between children and adults as well as those between normal children and children with rheumatic heart disease are discussed.

EFFECT OF PROLONGED EXERCISE ON POLYNUCLEAR COUNT IN MAN. J. J. BOOKMAN and D. J. FRAAD, Proc. Soc. Exper. Biol. & Med. **33**:183 (Oct.) 1935.

Fourteen members of a football team were studied throughout the season. In no case did the polymorphonuclear count show any significant alteration during the period of prolonged exercise in this ten weeks' study.

HANSEN, Minneapolis.

ANAEMIA WITH BONE CHANGES IN THE SKULL. WILFRID SHELDON, Proc. Roy. Soc. Med. **29**:743 (May) 1936.

Anemia was reported in a twin aged 2¼ years. The child was pale and small, with a muddy complexion. Roentgenograms of the skull showed thickening and increased density of the frontal and parietal bones only. The other bones showed no abnormality. The spleen was not enlarged, and there was no enlargement of the superficial lymphatic glands.

Several blood counts accompany the report. WILLIAMSON, New Orleans.

PURPURA HEMORRHAGICA: SPLENECTOMY. BERNARD MYERS, Proc. Roy. Soc. Med. **29**:750 (May) 1936.

The patient was presented before the clinical section of the Royal Society of Medicine on Nov. 13, 1931 (*Proc. Roy. Soc. Med.* [*Clin. Sect.*] **25**:154, 1931).

The capillary resistance test has given negative results since the operation, and the bleeding time was normal. The child had been in excellent health since the operation.

WILLIAMSON, New Orleans.

BLOOD PRESSURE IN CHILDREN. K. FRÖHLICH, Ann. pædiat. **152**:52 (Oct.) 1938.

In 444 children in bed convalescent after scarlet fever and diphtheria Fröhlich and co-workers found differences in blood pressure readings similar to those in 83 children examined by them in homes. This agrees with their observations on blood pressure in normal children. They therefore decline to acknowledge any connection between scarlet fever or diphtheria and an elevation of blood pressure. They considered blood pressure as definitely raised (Catel) if it surpassed the normal fixed by Katzenberger's formula (80 + 2X times) by at least 20 mm. According to this rule they found among 527 children 38 with hypertonia, i. e., 5.9 per cent. If certain ones are omitted from account—1 child who possibly had scarlatinal nephritis, a second whose condition was caused by congenital syphilis and a third whose condition was due to mitral stenosis—there remain 28 children with essential hyperpiesis, i. e., 5.3 per cent. Among 444 patients in the hospital there were 19 with hypertonia, i. e., 4.3 per cent; among 83 children in a home, 12, i. e. 13.25 per cent.

FROM AUTHOR'S SUMMARY.

SEQUENCE OF THE EXTENSIVE AND HEALING TENDENCIES OF SKELETAL CHANGES IN GAUCHER'S DISEASE, TOGETHER WITH OBSERVATIONS ON THE APPEARANCE OF TYPICAL PIGMENTATION. C. DE LANGE, Ann. pædiat. **152**:87 (Nov.) 1938.

Two girls with Gaucher's disease were kept under supervision for nine years. The spleen was removed in the younger one (E.) at the age of 3½ years. In this child the skeletal changes were less general than in the elder sister (A.), on whom no operation was performed. The fear, therefore, that splenectomy would promote the accumulation of kerasin in the bone was not proved by de Lange's observations. Both in the child who was operated on (E.) and in the one who was not operated on (A.) there followed severe destructions in the left hip joint and in the left tibia, perhaps in E. to a lesser degree than in A. The healing tendency of these processes is remarkable.

In the first years after splenectomy the liver increased in size; in the last years, however, this increase ceased.

The typical pigmentation appeared in both girls after some years. A. was 11½ years old and E. 10 years old when this became noticeable, and another interesting fact is that the discoloration has disappeared again in the younger child.

Both girls are backward in growth, particularly the younger. It must, however, be stressed that the healthy father is also somewhat undersized.

FROM AUTHOR'S SUMMARY.

DIFFERENTIAL DIAGNOSIS OF HEPATOSPLENIC SYMPTOM COMPLEXES WITH SPECIAL REFERENCE TO GAUCHER'S DISEASE. F. GOLDMANN and M. STEIN-FREIBERG, Ann. pædiat. **152**:224 (Jan.) 1939.

A girl of 7½ years living in a subtropical climate, who had fallen ill at the age of 2, tired easily and had frequent attacks of nosebleed of prolonged duration, slight icterus of the scleras and an increasing enlargement of the abdomen due to enlargement of the liver and spleen. All tropical diseases were gradually excluded by tests. The blood showed hypochromic anemia with slightly increased fragility of the red corpuscles, thrombopenia and an increased number of granulocytes, and there was increased excretion of urobilinogen in the urine. The van den Bergh reaction (indirect) was positive. The diagnosis of hemolytic anemia was doubtful on account of the absence of microcytes and because no occurrence of hemolytic jaundice in the family was known.

In order to elucidate the disease, which presented in its course several crises, bone marrow was obtained by puncture, and typical Gaucher cells were found.

The diagnosis of Gaucher's disease was confirmed when after splenectomy the typical cells were detected in the spleen.

Recovery followed without complications. During three months' observation there have been no signs of the illness. The value of an examination of the bone marrow in the differential diagnosis of a hepatosplenic complex of symptoms in childhood is emphasized, because the hemologic findings are not always characteristic.

FROM AUTHORS' SUMMARY.

SERUM PHOSPHATASE. YIEH and WISSLER, Ann. pædiat. **152**:248 (March) 1939.

In rickets serum phosphatase shows no special change. Vitamin D shock therapy produces varied pictures. In some instances serum phosphatase is lowered to normal in a week. In renal rickets serum phosphatase usually is high, but rarely it is lower and there is glycosuria. In dystrophy serum phosphatase may be lowered but is not necessarily so.

LESLIE, EVANSTON, ILL.

DIFFICULTIES IN DIAGNOSING TYPICAL LEUKEMIA IN A NINE YEAR OLD CHILD. C. HIRSCHBERGER, Ann. pædiat. **153**:43 (April) 1939.

A girl of 9 years had fever, anemia, leukopenia with relative lymphocytosis, moderate swelling of lymphatic glands and slight enlargement of the spleen without pathologic findings in other organs. All the serologic, bacteriologic and roentgenologic investigations gave negative results. The diagnosis of "aplastic anemia" was made on the temperature, the blood status and the absolute well-being. The enlargement of the spleen and lymphatic glands disappeared completely. After three months the picture of acute lymphatic leukemia developed with the typical blood status and a tendency toward hemorrhages, and a great number of lymphatic nodes became easily palpable. Biopsy and autopsy confirmed the diagnosis.

The special points in this case were that the anemia was always of a moderate degree, that, following a small wound caused by a bite, an ulcer formed which would not heal and that, further, a macular rash appeared. One of the child's uncles died a few years before this from lymphosarcomatosis. It was not possible to trace a lymphatic diathesis in the family.

FROM AUTHOR'S SUMMARY.

BLOOD TRANSFUSION IN CHILDREN. H. SCHAFFA, Ann. pædiat. **153**:177 (July) 1939.

Blood transfusion, no matter in what way it is used, is nowadays one of the best and most successful of therapeutic methods. The technic and accomplishment are simple, provided that all the prescribed precautions are taken and the correct donors chosen—apart from the disagreeable but not very dangerous accidents which are sometimes observed. Although the indirect method with citrated blood is used almost exclusively, the results in various diseases are very satisfactory. Failure, however, cannot always be prevented.

In the hospital where Schaffa's observations were made, with 60,277 very sick children, 400 transfusions have been given. In 68 cases the lethal end was not prevented. In most cases of leukemia and of septic processes with a hemorrhagic diathesis the effect of transfusion was transitory and sometimes only prolonged the duration of the illness. In cases of alimentary intoxication in infants results from transfusion are obtained only after dehydration is overcome. Transfusion is contraindicated in diseases of the cardiac valves with decompensation and in ulcerative endocarditis. The best results are obtained in alimentary and in secondary anemia. Favorable results, however, are also obtained in bronchopneumonia, empyema, pulmonary abscess, pyuria, fevers, colitis, marasmus, dystrophy and illness with a hemorrhagic diathesis.

The success of blood transfusion is based not only on substitution and alteration of the quality of the recipient's blood; the transfused blood also invigorates, changes and increases the resistance of the recipient organism and stimulates the activity of the bone marrow. The frequently life-saving effect of transfused blood demands that in every instance of serious disease blood transfusions should not be neglected.

FROM AUTHOR'S SUMMARY.

ADAMS-STOKES SYNDROME IN INFANCY. B. FAESSLER, Ann. pædiat. **153**: 327 (Sept.) 1939.

Eight cases of the Adams-Stokes syndrome in infancy and childhood are listed from the literature. Of the 8 children, 4 died between 6 days and 3 months of age; in some of the others the attacks became rarer, while in still others they stopped altogether. In 7 patients the heart block was congenital; in 1 patient it was acquired. The clinical and the postmortem diagnosis were six times "defective interventricular septum," once "open ductus Botalli" and once "persisting foramen ovale." If one can draw conclusions from such a small number of cases, there seems to be a connection between the Adams-Stokes syndrome and a defect in the interventricular septum which has not yet been demonstrated. The specific muscular system was histologically examined in only 2 cases. In both cases an interruption was found in the connecting auriculoventricular tissue between the atrioventricular node and the bundle of His; in 1 case, in addition to that, another interruption occurred between the bundle and the left branch.

In a 7½ month old boy with morbus caeruleus observed by Faessler, the first attack of the Adams-Stokes syndrome occurred at the age of 6 months. The pulse rate in the interval between attacks was 120 to 140. The electrocardiogram was normal. During the attacks the pulse rate went down to 22, while the electrocardiogram showed partly an atrioventricular rhythm and partly a changing between a sinus rhythm and an atrioventricular rhythm, while in all the other cases atrioventricular block was found. At the postmortem examination a transposition of the large vessels was found, a double arch of the aorta, stenosis of the pulmonary valve, a subaortal defect in the interventricular septum and an open foramen ovale. The connecting auriculoventricular tissue was normal. A striking feature was the thickening of the intima in the main artery of the sinus node.

The Adams-Stokes attacks in this child can be explained by the fact that the blood supply of the sinus node was so poor during exertion, owing to the narrow lumen of its main artery, that the formation of stimuli was much slowed down and by the fact that the atrioventricular node took over the lead. The anoxemia increased on account of the slow frequency of the heart, and the lack of oxygen in the brain produced unconsciousness and convulsions. As this occurrence was reversible a functional disturbance in the region of the sinus node had to be suspected clinically.

FROM AUTHOR'S SUMMARY.

TRANSITORY BRADYCARDIA DURING ACUTE RHEUMATIC CARDITIS IN CHILDREN. L. EDÉN, Ann. pædiat. **154**:48 (Oct.) 1939.

Among 258 children with acute rheumatic carditis 73 (more than 25 per cent) have shown transitory bradycardia, generally during the first three weeks of their illness. The bradycardia was caused by heart block only in 1 child; in the others sinus bradycardia was present. The symptom seems to be more common than is generally pointed out, and it can be of diagnostic significance but most probably is not of prognostic value.

FROM AUTHOR'S SUMMARY.

RESPIRATORY ARRHYTHMIA IN HEART DISEASE. K. KUHNE, Monatschr. f. Kinderh. **66**:7 (June) 1936.

In an effort to relate changes in respiratory rhythm to cardiac disease, including a study of two hundred electrocardiograms, Kuhne concludes that the study of

respiratory arrhythmia offers no assistance in diagnosis or prognosis. Respiratory arrhythmia is always present until the pulse rate runs up over 135 to 140. In other words, the phenomenon is affected not by the state of the muscle but by the frequency of the beat.

GERSTLEY, Chicago.

CONGENITAL RHABDOMYOMA IN SIBLINGS. WALTER PAULI, Monatschr. f. Kinderh. **66**:22 (June) 1936.

A case report is given, with roentgenograms showing rhabdomyomatosis of the heart in 2 siblings. The clinical and pathologic findings are described.

GERSTLEY, Chicago.

FAMILIAL NUCLEAR ANOMALY OF THE LEUKOCYTES OF PELGER AND HUET. C. J. Roos, Nederl. tijdschr. v. geneesk. **80**:1906 (May 2) 1936.

Roos describes a family of which twenty-one members showed the anomaly of the polymorphonuclear leukocytes described by Pelger (1931) and by Huet (1931). The predominant features of this anomaly are the large increase of the band-shaped leukocytes and the deviating form of the polymorphonuclears. This description brings the number of families in Holland showing this anomaly and observed since the first observation by Pelger to seven. In a girl of 6 years of this family the deviations of the blood picture were studied during scarlet fever and in her father during lobar pneumonia.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of Nose, Throat and Ear

CLIMATIC FACTOR IN MASTOIDITIS. N. D. FABRICANT, Arch. Otolaryng. **30**:549 (Oct.) 1939.

Fabricant presents 5 cases illustrative of the influence of weather and season on the clinical course of mastoiditis. It is noted that the disease is most frequently precipitated in the wake of a fall in atmospheric temperature (a "polar front"), when the functional status of the mucous membrane of the nose and throat has changed.

GREENWOOD, Chicago.

CERVICAL ABSCESS RESULTING FROM UNUSUAL FOREIGN BODY IN THE PHARYNX. L. E. ETTER, Arch. Otolaryng. **30**:631 (Oct.) 1939.

A case of confusing coincident symptoms is presented, in which an abscess in the cervical glands, apparently a localization secondary to a recurrent infection of the throat, turned out to be an abscess caused by swallowing a stalk of June grass. The importance of constantly bearing in mind such an unusual possibility in the differential diagnosis and etiologic study of cervical abscess is stressed.

GREENWOOD, Chicago.

FACTUAL BACKGROUND FOR THE TREATMENT OF PROGRESSIVE DEAFNESS FROM OTOSCLEROSIS. E. P. FOWLER, Bull. New York Acad. Med. **13**:667 (Dec.) 1937.

Otosclerosis is usually the result of systemic defects in metabolism, although by the time deafness is recognized there may be little or no chemical evidence of such defects. It is very difficult with present knowledge to diagnose the disease prior to the onset of deafness. It is recommended that children of otosclerotic families be frequently examined, especially before the critical age of the onset of puberty. The examination should include careful studies of the chemical composition of the blood. Ankylosis of the stapes is indicative of metabolic derangement

of the organism, circulatory anomalies or infectious processes. Care of such disturbances in the early stages may prevent the onset of deafness. In some cases in which otosclerosis has progressed to the stage of severe deafness surgical intervention may prove helpful.

JAHR, Omaha.

NEW TECHNIQUE IN THE SURGICAL TREATMENT OF SEVERE AND PROGRESSIVE DEAFNESS FROM OTOSCLEROSIS. M. SOURDILLE, Bull. New York Acad. Med. **13**:673 (Dec.) 1937.

Sourdille describes tympanolabrinthopexy, a surgical procedure which consists in associating the opening of the external semicircular canal to the new tympanic system derived from the normal system.

JAHR, Omaha.

ACUTE INFECTIVE LARNYGOTRACHEOBRONCHITIS. B. GREEN and E. P. MILLER, J. A. M. A. **109**:1903 (Dec. 4) 1937.

In a girl 17 months old with laryngotracheobronchitis intubation was attempted and failed. Tracheotomy was done, and a 1:1,000 solution of epinephrine was administered through the tracheotomy tube to relieve obstruction by the plugs of mucus in the trachea. The patient passed through a stormy two and a half weeks' siege before the tube could be removed. The epinephrine appeared to exert a life-saving action on the edematous mucosa when administered directly to it.

HEERSMA, Kalamazoo, Mich.

DIAGNOSIS AND TREATMENT OF INFANTILE MASTOIDITIS. P. W. LEATHART, Brit. M. J. **2**:723 (Oct. 7) 1939.

A discussion of mastoiditis occurring in infancy is outlined. The physical signs and symptoms and laboratory tests for the disease are mentioned. The point is stressed that some infants succumb to rather evasive diseases which in fact have their origin in unrecognized mastoiditis. The condition is considered far more frequent by the author than has hitherto been believed. It is thought that early diagnosis can be made with confidence and that early operation can save a large percentage of these patients. The author states that babies should never be nursed or fed lying on their backs (this point is not made clear by him).

ROYSTER, University, Va.

MAXILLARY SINUSITIS IN THE SMALL CHILD. J. C. OREGGIA, Arch. de pediat. d. Uruguay **10**:197 (April) 1939.

Two forms of maxillary sinusitis are described, an osteomyelitic form in the young child and a purulent form in the older child, usually following infectious diseases.

Oreggia observed 3 patients with the osteomyelitic form, all children 6 years of age. The condition in each child was due to staphylococcic infection. Two of the children responded to surgical treatment; the third child died, the condition being of a malignant type. The classic symptoms of the osteomyelitic form are: marked swelling of the internal angle of the eye and of the upper jaw accompanied by profuse nasal drainage.

The author has seen no definite connection between adenoiditis and sinusitis. Many of the children with sinusitis are children who are affected with a constitutional diathesis. These children continue to have sinus disease in spite of the removal of tonsil and adenoid vegetation. They suffer from chronic and mucopurulent catarrh. Often they have prolonged subacute febrile manifestations. There is usually much postnasal drainage. The mucous membranes of the nasal fossae are often pale and atrophic.

Removal of the adenoids does not always cure the sinusitis and the prevailing repetitional attacks.

The author advises against puncture of the maxilla and washing of the sinuses. If a permanent window has to be made, the gingivolabial route is preferred to the intranasal. As a local treatment the author advises nasal shrinkage with cocaine and suction, together with local use of antiseptics or antivirus preparations.

SCHLUTZ, Chicago.

Diseases of Lungs, Pleura and Mediastinum

SULFAPYRIDINE IN THE TREATMENT OF LOBAR AND BRONCHOPNEUMONIA IN INFANTS AND CHILDREN. J. M. DOBBINS, H. RAPPAPORT and M. A. BRESCICI, Arch. Pediat. **56**:375 (June) 1939.

Twenty-seven infants and children suffering from pneumonia were treated with sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine), with one death.

Two patients showed a spread of the pneumonic process while under treatment with sulfapyridine.

All the diagnoses were confirmed by roentgen examination, and typing was obtained in 15 cases.

Responses to sulfapyridine therapy occurred within forty-eight to seventy-two hours, and there were no untoward effects from the use of the drug.

ORR, Buffalo.

SULFAPYRIDINE: METHOD OF USE IN THE PNEUMONIAS OF CHILDHOOD. M. R. REYNOLDS and L. B. SLOBODY, Arch. Pediat. **56**:415 (July) 1939.

Sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine) when properly used in the treatment of the pneumonias of childhood characteristically brings about a precipitous fall in temperature, followed by a disappearance of toxicity and a return of the respiratory rate and general condition to normal. The signs of consolidation may persist for the usual length of time. Convalescence is markedly shortened, and complications appear to be rare.

Children require relatively large doses of the drug. Infants require a further 50 per cent increase in the size of the dose on the basis of body weight to bring about results comparable with those obtained in older children.

ORR, Buffalo.

SULFAPYRIDINE IN THE TREATMENT OF PNEUMONIA IN INFANCY AND CHILDHOOD. A. T. WILSON, A. H. SPREEN, M. L. COOPER, F. E. STEVENSON, G. E. CULLEN and A. G. MITCHELL, J. A. M. A. **112**:1435 (April 15) 1939.

In a series of 70 cases of pneumonia, not classified as to type of pneumonia or pneumococci, half the patients were treated with sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine) and half were controls, without specific treatment. The usual daily dose was 1 grain (0.064 Gm.) per pound of body weight after a large initial dose. The blood level of the drug was closely followed. There were no deaths in either group. Sulfapyridine shortened the course of the pneumonia by three to four days, as evidenced by fall in temperature and clinical recovery. The best results were obtained with a blood concentration of 1 mg. per hundred cubic centimeters. Two patients were apparently unaffected by the drug. Two others had relapses after the administration of the drug was discontinued. Mild reactions were present, chiefly vomiting and cyanosis, which were also seen in the controls. No severe reactions were encountered. HEERSMA, Kalamazoo, Mich.

ACTION OF ANTIPNEUMOCOCCUS SERUM IN THE PNEUMONIC RAT AND ITS PENETRATION INTO THE PULMONARY LESION. A. H. KEMPF and W. J. NUNGESTER, J. Infect. Dis. **65**:1 (July-Aug.) 1939.

In pneumonic rats, with and without serum therapy, large numbers of pneumococci were found in the lungs; in the untreated animals they were also found in the blood, spleen, liver and kidneys. That is to say, the administration of antipneumococcus serum tended to keep the blood and other organs free of pneumococci but did not reduce the number of bacteria in the lung. If treatment was delayed until after the organisms were distributed throughout the body, the antiserum was effective in clearing the blood stream, but the number of pneumococci in the spleen, liver and kidneys was little different from that of an untreated animal. Moreover, the blood stream did not remain free of bacteria.

Circulation persists in the pneumonic lung, but it is possibly much slower than normal. In experiments carried out with a rabbit hemolysin serum of high titer, it was found that the antiserum is not able to penetrate the alveoli of the lung to a demonstrable extent. Much more antiserum is necessary to neutralize the polysaccharide present in the alveoli of the lungs than the extremely small amount which may penetrate. This is reflected by the fact that antiserum does not decrease the number of pneumococci in the pneumonic lung.

(TOOMEY, Cleveland.) FROM AUTHORS' SUMMARY.

PNEUMONIA SERUM THERAPY IN INFANTS AND CHILDREN: ILLUSTRATED BY A CASE OF TWINS WITH TYPE XIV PNEUMONIA. R. L. NEMIR, M. Clin. North America **23**:635 (May) 1939.

Since the identification of the heterogenous pneumococci in group IV, to which over 50 per cent of the cases of pneumonia in childhood are due, and the division of the group into types IV to XXXII, the serum treatment of this disease has been greatly advanced by the production of specific serums for many of the types of organisms isolated. It has also been possible to determine the differences in virulence of the various types and to appraise the efficacy of serum treatment with greater accuracy.

The evaluation of the severity of disease in relation to the type of pneumococcus is important. Types I and XIV are usually associated with definite severe pneumonia. Types VI, XIX, often III, and many of the higher-numbered types are usually associated with mild disease of short duration. Because of the frequent occurrence of these types in the nasopharynx in normal persons, repeated pneumococcus typing should always be done when these organisms are found. Severely ill patients in whom types VI and XIX are present often have bronchopneumonia with other organisms, such as hemolytic streptococci, associated. Cases of pneumonia due to type XIV show a high incidence of bacteremia and pleurisy. Nemir's experience with the use of serum for infections with types I and XIV and for infections with V and VII has been encouraging, especially since the serum seems definitely to shorten the disease and, if given early, to lessen the incidence of empyema.

The value of serum for pneumonia due to type XIV is illustrated in 2 cases. The patients were twins 14 months of age, both suffering from severe forms of the disease. The crisis occurred in the serum-treated one within four days, and he was discharged on the seventh day after admission. The second child was severely ill for nine days, and the crisis occurred on the thirteenth day of the disease.

In serum treatment of pneumonia in children the initial dose should always be small, not more than 1 to 2 cc. This should be diluted with physiologic solution of sodium chloride and given slowly intravenously. A second injection is given after two hours, and subsequent injections, at four to six hour intervals. One injection should be given intramuscularly after the temperature has been normal

for from four to six hours. If marked improvement follows the first two intravenous injections, other injections may be given at four to six hour intervals intramuscularly. EUGENE H. SMITH, Ogden, Utah.

BENIGN IDIOPATHIC PNEUMOTHORAX IN A CHILD, WITH RECURRENCE. B. BAIZE, Arch. de méd. d. enf. **42**:575 (Sept.) 1939.

Galliard in 1888 established nontuberculous pneumothorax in the adult as a distinct entity. A type has also been described by Palmer and Taft and De Verbizier in which recurrences are common, the first attack usually being coincident with some violent effort.

In children, however, this disease is extremely rare, and cases are usually reported in the category of nontuberculous or spontaneous pneumothorax. Several valuable monographs have been contributed on this subject by Lereboullet, Lelong and others; the reports show that in most instances pneumothorax has been a sequel of some acute invasion such as pneumonia, whooping cough or pulmonary abscess, while in other cases it could be attributed to congenital sources. In a series of 42 cases reported by Lereboullet there were 21 fatalities, a mortality of 47 per cent. There remains a form of pneumothorax in the newborn in which the cause is obscure and in which recurrences have not been noted.

Baize reports a case of pneumothorax in a boy of 13, induced by violent effort in the gymnasium. There were two recurrences, at 3½ months and 3½ years, respectively, but examination three years after the second episode revealed in every respect a normal respiratory apparatus. AMESSE, Denver.

HYDATID CYST OF THE LUNG. COSACESCU and MARCULESCU, Bull. Soc. de pédiat. de Iasi **9**:24, 1938.

The patient, 7 years of age, had the appearance of a child of 4. Examination revealed dulness over the lower portion of the left lung and absence of breath sounds. After exploratory puncture, a large amount of gelatinous material and pus was removed, together with the cyst membrane. The diagnosis was echinococcus cyst of the lung. The postoperative course was good, and it was hoped that improved growth and development of the child would follow. LESLIE, Evanston.

RELAPSING NONTUBERCULOUS SPONTANEOUS PNEUMOTHORAX IN A BOY. P. BAIZE, Bull. Soc. pédiat. de Paris **37**:81 (Feb.) 1939.

A boy 13½ years old had pneumothorax in the right side of the chest twice within a little over three months, and once more in the left hemithorax three and a half years later. Each time there was little or no effusion, and it cleared rapidly. His general condition was good. No evidence of pulmonary tuberculosis was found. His tuberculin reaction was positive. A theoretic explanation is that some congenital malformation of terminal bronchioles might have given rise to subpleural bullous emphysema, over which the thin pleura ruptured on slight provocation. BENJAMIN, Montreal, Canada.

Diseases of the Gastrointestinal Tract, Liver and Peritoneum

CLINICAL OBSERVATIONS RELATING TO THE NORMAL AND ABNORMAL FRENUM LABII SUPERIORIS. JOHN E. TAYLOR, Am. J. Orthodontics **25**:646 (July) 1939.

Taylor examined 516 grade school children, aged from 5½ to 11, and 1,067 high school children, aged from 12 to 18, to determine whether a maxillary diastema is a normal condition in children of 5 or 6 years of age and whether

the space normally closes after the eruption of the lateral and canine teeth. This survey confirms the statement of Mershon and the investigations of Lewis that it is a normal condition.

LEWIS, Dayton. [ANGLE ORTHODONTIST]

SIGNIFICANCE OF GASTRIC ACIDITY AFTER HISTAMINE STIMULATION: A STATISTICAL STUDY OF 2877 GASTRIC ANALYSES, J. M. RUFFIN and M. DICK, Ann. Int. Med. **12**:1940 (June) 1939.

The range in gastric acidity following histamine stimulation in normal persons was found to be much greater than that which followed the ingestion of an Ewald meal. When free hydrochloric acid was present after the administration of histamine, the actual level of gastric acidity was considered of no diagnostic importance.

READING, Galveston, Texas.

THE ACUTE ABDOMEN IN CHILDHOOD. HERZFELD, Edinburgh M. J. **46**:750 (Dec.) 1939.

Herzfeld relates experiences in the Hospital for Sick Children, Edinburgh, during the previous ten years. Among 4,741 newly admitted patients there were 753 children (16 per cent) who underwent abdominal operation. Appendicitis was found in 498 of them; intussusception, in 107. The next two common diseases proved to be abdominal tuberculosis, in 43, and peritonitis, in 32. This leaves 73 children with less common conditions, which the author enumerates.

Herzfeld states that appendicitis is relatively as frequent in children as in adults. Perforation and early peritonitis are not unusual in children whose symptoms date back only twelve to twenty-four hours, and 71 per cent of all the patients with these conditions require drainage. If the temperature rises to 104 F. or above, the presence of appendicitis can usually be excluded. The mortality rate for this disease is 2.4 per cent for the entire period of childhood.

Intussusception occurred in the first two years in 81 per cent of the children with this condition. It occurred in twice as many boys as girls, but the death rate in girls was twice that in boys. The author emphasizes the fact that the first stools after the onset of symptoms may not contain blood, the appearance of which may be delayed several hours. The early diagnosis should not be retarded for such a reason. In the first stage a barium sulfate enema may reduce the invagination, during which the barium sulfate can be seen by means of the fluoroscope to pass back through the ileocecal valve. However, operation is more certain, as it insures a complete reduction.

The 43 children with acute abdominal tuberculosis were admitted as requiring emergency attention, and these patients have been as frequent as formerly, while those with the chronic condition have become much fewer. It is difficult before operation to differentiate between acute appendicitis and tuberculosis of the ileocecal lymph glands. In tuberculous peritonitis a much more serious disease is encountered; the preliminary symptoms have been those of obstruction.

Primary peritonitis is relatively rare; of 32 infections, 20 were due to Streptococcus, 11 to Pneumococcus and 1 to Staphylococcus.

NEFF, Kansas City, Mo.

ENLARGED ABDOMEN. ? HEPATOMEGALY. U. SHELLEY, Proc. Roy. Soc. Med. **32**:1374 (Sept.) 1939.

A boy of 21 months had developed normally until the age of 12 months. Sometime between the twelfth and the fourteenth month the stools became offensive, the appetite commenced to wane, the teeth began to crumble, and the abdomen was noticed to be growing large. On admission to the hospital the only abnormal sign was a large liver, which was firm and smooth. The child was kept in the

hospital for about a month. After his discharge the abdominal girth decreased by 1 inch (2.5 cm.), the teeth were cut, and the child began to walk.

Two full investigations were made six months apart, and the results are reported.

WILLIAMSON, New Orleans.

FEBRILE FORM OF INTESTINAL OBSTRUCTION BY MECKEL'S DIVERTICULUM. J. CATHALA, P. MARTROU and L. GRAS, Bull. Soc. pédiat. de Paris **37**:92 (Feb.) 1939.

A 4 month old boy died three and a half days after the onset of symptoms of strangulation of the terminal part of the ileum. This was due to kinking by a Meckel's diverticulum, which extended as a cord from the free surface of the intestine to the anterior pelvic wall just above the bladder. This was revealed at necropsy. There was no peptic ulcer in the diverticulum. The infant was not operated on because of fever, absence of blood in the stools, the crying spells which usually accompany colicky pain, and the good general condition for the first forty-eight hours. There was apparently a slow insidious development of signs of obstruction, the chief one being abdominal distention, at first of the lower part and later of the entire abdomen.

BENJAMIN, Montreal, Canada.

METABOLIC RELATIONS BETWEEN THE EXUDATIVE DIATHESIS AND ALIMENTARY TOXICOSIS. F. GOLDMANN, Ann. pædiat. **152**:160 (Dec.) 1938.

Clinical observations and metabolic investigations demonstrate that there exist common changes, estimated by the sodium-chlorine quotient, in clinically different conditions of infancy, such as generalized eczema, the acidosis of dypepsia and the state in the first few months of premature life. These changes concern the mineral metabolism in the sense of a "transmineralization" into the tissues and they become clinically apparent as a tendency toward edema.

It therefore seems justifiable to speak of a general disturbance of permeability in all these conditions and to use the retention of sodium in the urine as a valuable test for dysergy. This is to be understood in early infancy not as a pathognomonic criterion of an illness in itself but rather as a nonspecific symptom of functional cellular debility. It is assumed that the cause of the disturbance of permeability is azotemia, as has been proved in all these conditions by repeated investigations. The question of electrolytic changes in the tissues, measured on the electrometrically found drop in potential (Keller), is discussed in this connection.

FROM AUTHOR'S SUMMARY.

THE TAKATA REACTION AS AN AID TO PROGNOSIS OF HEART DISEASE IN CHILDHOOD AND OF NUTRITIONAL DISTURBANCES IN INFANTS. W. HIRSCH, Ann. pædiat. **152**:316 (March) 1939.

The Takata reaction in infancy is not only a test of liver function. The reaction is positive—on account of the greater lability of the juvenile organism—in all cases of serious disease in which the detoxicating function of the liver is disturbed or in which the colloidal state of the blood serum is at all changed (typhoid, pneumonia, nephritis, septicemia, serious infection).

The reaction shows itself as an aid to prognosis in cases of heart disease in childhood, considered with the rest of the clinical picture, the reaction generally running parallel with the sedimentation rate. A positive result is found only in cases of very serious disease of the heart. The prognosis is more favorable with a negative reaction. Particularly favorable is a change from positive to negative during the course of treatment.

Of the diarrheic diseases in infancy, simple dyspepsia is associated with a negative reaction, while the reaction is always positive when the disturbance is more serious and when there is alimentary toxicosis.

The reaction is generally negative in the presence of dysentery in an infant, because the illness is more localized.

FROM AUTHOR'S SUMMARY.

EXCRETION OF UROBILIN AND STERCOBILIN IN WELL CHILDREN BEFORE AND AFTER ADMINISTRATION OF DECHOLIN (BILE ACIDS). K. T. SIMON, Ann. pædiat. **152**:338 (March) 1939.

A short survey is given of the physiology and biochemistry of bilin. The necessity is stressed of considering the factors which may influence the excretion of bilin, e. g., intestinal disturbances, nutritional difficulties, destruction and regeneration of the blood, diseases of the liver, and other conditions.

The normal rate of excretion of bilin was not higher as a rule than 2 mg. per day for urobilin, 20 mg. per day for stercobilin and 20 mg. per day for total bilin. It is probable that urobilin is excreted according to an individual cycle, which may be modified by special other factors, such as the intake of food.

No increase in the excretion of urobilin could be detected after administration of decholin to children without hepatic disease. If decholin really has a "squeezing" influence on the liver, it has to be assumed that the healthy liver does not contain any stores of urobilin. FROM AUTHOR'S SUMMARY.

TRACHEOESOPHAGEAL FISTULA. J. C. SCHIPPERS, Monatschr. f. Kinderh. **80**:130, 1939.

This is a case report with a photograph showing a commonly found abnormality, a blind ending of the upper part of the esophagus and a connection between the trachea and the lower portion of the esophagus. GERSTLEY, Chicago.

PROBLEMS OF EXSICCOSIS IN INFANTILE TOXICOSES. V. WHER, Ztschr. f. Kinderh. **61**:135 (Aug. 9) 1939.

It is generally agreed that toxicosis is the result of exsiccosis plus toxic influences.

Wher studied changes in the metabolism of water and minerals by examining the livers of children who had died of toxicosis and by examining the content of vesicles produced by cantharides applied to the skin. He discusses the shift in mineral balance which explains the dehydration, the acidosis and the inability of the tissue to retain water. In mild toxicosis only extracellular water is lost (intracellular water may be increased). Sodium and potassium ions, which have hydrating effects, are decreased, while calcium and magnesium ions, which have dehydrating effects, remain rather constant. Electrostatic factors also play a role in the disturbances of water and mineral metabolism. SIEMSEN, Chicago.

ACUTE PANCREATIC NECROSIS WITH GASTRIC PERFORATION IN A CHILD. F. GROSS, Ztschr. f. Kinderh. **61**:142 (Aug. 9) 1939.

About a dozen lesions of this type are recorded in the literature. Most of these lesions presented a dramatic onset, but none was diagnosed correctly. The author describes a case in detail, in which the clinical picture was noncharacteristic. The cause is indefinite. Presumably reflux of bile or of intestinal secretions through the pancreatic duct causes activation of trypsin and digestion of pancreatic tissue and of adjacent gastric tissue. The obstruction causing the reflux may be in the form of a gallstone, an ascarid or a spasm. SIEMSEN, Chicago.

EXOGASTRIC FIBROMA WITH GASTROINTESTINAL HEMORRHAGES. E. FILO and F. SUBIK, Acta med. Scandinav. **101**:34, 1939.

Among the rare causes of gastrointestinal hemorrhages is exogastric fibroma. Only a few cases are reported in the literature. Those cases were discovered only at operation or autopsy. The authors report a case. A 14 year old was anemic and had had occult bleeding for two years. He was first treated

with roentgen radiation for aleukemic leukemia, because the mass under the left costal margin was mistaken for the spleen. Later the diagnosis was changed to thrombophlebitis of the splenic vein and splenectomy advised. During the operation the mass was found to be a pedunculated tumor of the large curvature of the stomach. Histologically, it was a fibroma originating from the submucosa and did not invade the mucosa of the stomach.

KAJDI, Baltimore.

Nervous Diseases

LYMPHOCYTIC CHORIOMENINGITIS: REPORT OF A FATAL CASE WITH AUTOPSY FINDINGS. T. E. MACHELLA, L. M. WEINBERGER and B. W. LIPPINCOTT, Am. J. M. Sc. **197**:617 (May) 1939.

What is believed to be a case of lymphocytic choriomeningitis is reported, with the clinical and laboratory findings and the observations at autopsy. The chief changes in the brain were those in the ventricular walls, choroid plexuses and basal meninges. No inclusion bodies were found. Death was due to respiratory failure secondary to an increase in intracranial pressure as the result of blockage of subarachnoid spaces at the base of the brain.

EMKE, Omaha.

SYMMETRIC CEREBRAL CALCIFICATION, PARTICULARLY OF THE BASAL GANGLIA, DEMONSTRABLE ROENTGENOGRAPHICALLY. L. McK. EATON, J. D. CAMP and J. G. LOVE, Arch. Neurol. & Psychiat. **41**:921 (May) 1939.

"We believe that the frequent association of tetany with symmetric cerebral calcification should be emphasized."

The authors report 6 cases. Two of the 6 patients had definite hypoparathyroid tetany. The question is brought up as to whether patients who show calcification associated with mental deterioration and convulsive seizures had hypoparathyroidism as a cause originally, which was not detected.

BEVERLY, Chicago.

ENCEPHALOPATHY FOLLOWING ANESTHESIA: HISTOLOGIC STUDY OF FOUR CASES. A. T. STEEGMANN, Arch. Neurol. & Psychiat. **41**:955 (May) 1939.

Four cases of postanesthetic encephalopathy in adults are reported. One patient received avertin with amylene hydrate, one received cyclopropane, and the other two received nitrogen monoxide and oxygen. The clinical signs were (1) disturbance in consciousness—stupor interrupted by periods of screaming, mania or hysteria-like behavior; (2) motor symptoms—restlessness, convulsions, twitchings; (3) decerebrate phenomena; (4) visual disturbances—hallucinations, color vision and blindness; (5) autonomic signs—variation in pulse rate, in blood pressure, in respiration and sweating, cyanosis and flushing; (6) hyperthermia.

The author concluded from anatomic studies that the changes in the brain were due to the deprivation of the nerve cells of oxygen.

BEVERLY, Chicago.

TREATMENT OF ACUTE ENCEPHALITIS BY THE INTRAVENOUS INJECTION OF HYPOTONIC SALT SOLUTION. G. M. RETAN, New York State J. Med. **39**:1774 (Sept. 15) 1939.

Retan reports the successful treatment of 15 patients for acute encephalitis by means of an intravenous injection of hypotonic salt solution and continual drainage by lumbar puncture. All of the patients have been completely relieved of all objective and subjective symptoms. A complete description of this method of treatment is given. In addition, 40 patients with chronic encephalitis have been treated by the same method, with definite improvement in 80 per cent.

AIKMAN, Rochester, N. Y.

THE BLOOD AND SPINAL FLUID SUGAR AND CHLORIDE CONTENT IN MENINGITIS. E. HENDRY, Arch. Dis. Childhood **14**:159 (June) 1939.

In the normal subject variations in the sugar content of the cerebrospinal fluid are dependent on variations in the sugar content of the blood, but changes in the latter are not immediately reflected in the cerebrospinal fluid. The lower limit for the sugar content of the cerebrospinal fluid normally is 50 mg. per hundred cubic centimeters, and the ratio of cerebrospinal fluid sugar to blood sugar is 0.6. In tuberculous meningitis the sugar content of the cerebrospinal fluid is reduced, as is also the ratio of cerebrospinal fluid sugar to blood sugar; the reduction in both becomes more marked as the disease progresses. If convulsions occur, the level of sugar in the cerebrospinal fluid may be raised to apparently normal limits, but the blood sugar is also raised, and the ratio of cerebrospinal fluid sugar to blood sugar remains below normal. In meningococcic meningitis, the cerebrospinal fluid sugar is reduced and may be almost entirely absent, and the ratio of cerebrospinal fluid sugar to blood sugar is below normal. As recovery takes place, the sugar content of the cerebrospinal fluid and the ratio of cerebrospinal fluid sugar to blood sugar return to normal. The chloride content of the cerebrospinal fluid is reduced in all forms of meningitis, but this reduction is due to reduction in the blood chloride content. Reduction in chloride, in the early stages of tuberculous meningitis is less constant than reduction in the cerebrospinal fluid sugar.

KELLY, Milwaukee.

RAPIDLY FATAL ENCEPHALITIDES IN CHILDREN. C. GARDÉRE, M. DAUVERGNE and G. BERTRAND, J. de méd. de Lyon **20**:281 (May 5) 1939.

Gardére and his associates point out that certain forms of encephalitis in children are noteworthy for their particularly rapid development and their exceptional gravity. The encephalitis with rapidly fatal termination is the one in which the evolution does not go beyond the third day. This encephalitis seems to appear especially in nurslings. Of 43 cases, 17 concerned infants of the first year; 9, those of the second year, and the other 17, children between the ages of 2 and 12 years. This encephalitis with rapid death is most frequently of the parainfectious type (34 of 43 cases). Whooping cough seems to be the most frequent causal infection during the first two years of life, and measles, during the later years. Varicella and vaccinia are less often the cause. In some cases the cerebral infection seems to be primary, and the cause is still obscure, but at times it may be of influenzal origin and at other times a connection with lethargic encephalitis may be considered. The symptomatic picture is characterized chiefly by convulsions, somnolence and coma. What is especially characteristic is the almost immediate appearance of symptoms indicating bulbar involvement: irregularity of the respiratory rhythm and tachycardia. Lumbar puncture usually yields a normal cerebrospinal fluid or one with a slight lymphocytic reaction. The anatomopathologic studies are as yet few, but they reveal the usual diffuse lesions of encephalitis with involvement of the bulbar centers, where cytologic lesions are found in spite of the rapidity of evolution. The diagnosis of the primary forms is especially difficult. In nurslings the possible presence of suppurating otitis or mastoiditis must be considered, for these may produce similar symptoms. The outcome of the hyperacute forms of encaphalitis is usually rapidly fatal, although occasionally the bulbar symptoms subside and the child recovers.

J. A. M. A.

MODERN CONCEPTIONS OF ALLERGY IN CHILDREN. A. E. LARGUIA, Día méd. **11**:431 (May 22) 1939; Medicos **1**:17 (Nov.) 1939.

Larguia discusses modern conceptions of the development, character and types of allergy in children. He uses the word "allergy" as a synonym of "hypersensitivity." The term covers all the specific allergic reactions which cannot be considered in the group of anaphylactic phenomena. According to the author, heredity

is the factor of primary importance in the development of allergy. From 40 to 60 per cent of the children who suffer from allergy come from families with a history of allergy, whereas only 5 per cent of nonallergic children come from such families. Children with a bilateral history of familial allergy have a great predisposition to the development of allergic diseases. The larger the number of cases of inheritance in the family the more marked the influence of heredity and the earlier the development of allergy in the children (Cook, Spain). Hyperallergic children frequently show reactions to the allergens to which the parents react (Woringer). The frequency of hereditary allergic transmission is twice as great in females as in males. It seems that the majority of allergic children belong to only one blood group. Hereditary transmission of allergy follows Mendel's laws. It is of a recessive character and either of a conceptional or germinal type, but the transmission may be congenital (transplacental) or may appear after birth or during early infancy. The conception of an intrauterine sensitization of a constitutionally predisposed fetus by proteins which pass through the placenta explains the early appearance of allergic eczema or asthma in the infant who is fed on the mother's breast alone. A larger number of children (more than 60 per cent) who suffer from allergic diseases give positive skin reactions to egg albumin and other antigens with which they have had no contact. A great number of such positive skin reactions, however, are due to potential sensitivity of the patients for the given antigen, as the patients have, at one and the same time, actual and potential sensitization. The allergic reaction depends on a constitutional predisposition of certain structures, namely, the skin, the nasal, bronchial and conjunctival mucosae, the digestive tract and possibly, also, the brain, the retina and the bladder, to experience a shock when they come in contact with a specific allergen. During the shock specific antibodies are produced which, in association with the allergens and in the presence of certain substances in the blood, cause the allergic symptoms. Heredity plays no part in the development of acquired allergy. In the course of acquired allergy, which is milder than hereditary allergy, the skin reactions are frequently negative or induced by larger doses of allergens, and frequently the antibodies cannot be identified in the blood of the patients. The diagnosis of acquired allergy is difficult. The treatment consists in eliminating contact with the given allergen. Certain hyperallergic patients who suffer from hereditary allergy may also suffer from acquired allergy.

CLINICAL PROBLEM OF MIGRAINE IN CHILDREN. A. OLIVEIRA LIMA, Brasil-med. **53**:765 (July 29) 1939.

According to Oliveira Lima, allergy is the main etiologic factor producing migraine in children. Of secondary importance are heredity and constitutional physical factors or pathologic factors. The condition is more frequent in girls than in boys and, again, is more frequent in girls of a nervous type than in normal girls. The clinical symptoms are those of the prodromal and aural periods, the attack and the after-attack period. The topographic pattern, acuteness and evolution of the disease vary in the different cases. The main symptom of the attack is the unilateral headache, which appears at regular or irregular intervals with pain of an oppressive, irradiating or neuralgic type; it is accompanied by nausea, vomiting and various sensory disturbances. Intolerance to light is more or less acute in all cases. The after-attack stage gradually establishes itself, after aggravation of the acute symptoms of the attack. It becomes evident by appearance of physical depression, sleep, disturbances in the secretion and elimination of urine, rhinorrhea and general dull pain. In some cases the development of an abortive or equivalent attack prevents occurrence of typical attacks. Chronic headache may be a late sequel to the disease. Treatments are of three types: (1) preventive, (2) symptomatic and (3) after-attack. There are two forms of preventive treatment: that in which patients are advised not to marry persons who are sensitive to the same allergens, and the actual preventive treatment of the patient, which

includes proper diet and avoidance of food and ambient allergens to which the patient is sensitive. Symptomatic treatment varies with the type of headache. The following general measures are indicated: The patient is confined to a dark quiet room, and drugs with a vasodilating action are administered during the prodromal and aural stages; during the attack, according to indications, drugs of vasoconstrictive action, or else analgesics, sedative drugs and especially ergotamine tartrate, are given. Caffeine, calcium and some other drugs can be resorted to when indicated. The after-attack treatment is a continuation of the symptomatic treatment with certain modifications. It consists of proper diet, rest, and administration of either sedatives or stimulants, according to indications.

J. A. M. A.

PROGRESSIVE CEREBRAL SCLEROSIS. I. ZIMÁNYI and I. FÉNYES, Orvosi hetil. **83**:262 (March 18) 1939.

The patient was a boy aged 10 years. At 6 years of age he was an intelligent, well behaved pupil. From that time on his mental development showed steady deterioration to dementia. Later tonic and clonic convulsions occurred, and the walking became ataxic. Now the boy is totally demented. The Wassermann reaction of the blood was always negative. An encephalographic study showed atrophy of the frontal gyruses. A microscopic examination of the brain tissues by cerebral puncture confirmed this diagnosis.

GÖTTCHE, Budapest, Hungary.

VITAMIN C CONTENT OF CEREBROSPINAL FLUID. I. GAMLO, Acta pediat. japon. **45**:1003 (July) 1939.

The vitamin C content of the cerebrospinal fluid was examined in 81 cases of tuberculous meningitis, 20 cases of epidemic cerebrospinal meningitis, 1 case of influenzal meningitis, 1 case of otitic pyogenic meningitis, 3 cases of pneumococcic meningitis, 1 case of staphylococcic meningitis, 12 cases of epidemic encephalitis, 1 case of postvaccination encephalitis, 1 case of herpetic encephalitis and 12 cases of meningismus. The 2,6-dichlorophenolindophenol reduction method was used, and no significant variations from normal values were found in these conditions.

KATO, Chicago.

Psychology and Psychiatry

PSYCHOLOGIC TYPES IN CHILDHOOD. R. GRÜNEBERG, Ann. pædiat. **152**:178 (Dec.) 1938.

After a survey of the present day problem of psychologic types of children, observations are made on the behavior patterns of children who present educational difficulties. The children are grouped into obstinate, babyish, shy and unchildish types. It is demonstrated that there are many transitional shades between these types and the normal ones. This study can be used for the psychologic understanding of normal children.

FROM AUTHOR'S SUMMARY.

PSYCHIATRIC HISTORIES OF CHILDREN. R. GRÜNEBERG, Ann. pædiat. **152**:328 (March) 1938.

Every diagnosis of a psychiatric condition in a child must be based on a systematic anamnesis. The technic of eliciting the anamnesis demands a consideration of the principles of child psychiatry, which includes psychiatric conditions in the family. Grüneberg communicates a scheme of anamnesis which has been found workable in practice. After introductory questions which are intended to

inform the partner in the anamnesis about its significance, the course of the child's development is followed through the divisions of (1) infancy, (2) toddler age and (3) school age, and in each case the physical and mental phenomena of that development and the deviations caused by the patient's surroundings are separately scrutinized. If this scheme of anamnesis is applied carefully, the material thus obtained can be used for scientific purposes.

FROM AUTHOR'S SUMMARY.

CAUSAL CONNECTION OF CURETTAGE FOR ABORTION TO MONGOLIAN IDIOCY. E. MAYERHOFER, Ann. pædiat. **154**:57 (Nov.) 1939.

According to Mayerhofer's experience, the influence of curettage undertaken as a measure of birth control is assuming an ever increasing importance among the factors responsible for mongolian idiocy. This is shown by the fact that often in the marriages of young persons, particularly a short time after curettage, mongolian idiots are conceived and born. This experience can be had particularly in town practice, far less in the country. The indirect cause seems to lie in the endometrium which is not completely healed after curettage. "Healthy fetuses are curetted and mongoloid ones are born afterward." The pediatrician may be able to counteract this special cause of mongolian idiocy by enlightening the parents in his family practice.

FROM AUTHOR'S SUMMARY.

Diseases of the Genitourinary Tract

TREATMENT OF VULVOVAGINITIS WITH ESTROGEN. CHARLES MAZER and FRED R. SHECHTER, J. A. M. A. **112**:1925 (May 13) 1939.

The authors discuss vulvovaginitis in children as to its etiology, diagnosis and glandular treatment. Their series of 118 children was treated with potent estrogens by hypodermic, vaginal and (in a few cases) oral routes. Hypodermic treatment produced cure in 78 of 81 cases, with 10 per cent recurrence. Vaginal instillation cured 33 of 34 patients, and there were no recurrences. There were no cures with oral treatment. Side effects, e. g., production of secondary sex characteristics, were negligible and transient. The conclusion is that a longer course of treatment (about eight weeks) is advisable to prevent recurrence.

HEERSMA, Kalamazoo, Mich.

GONORRHEAL VAGINITIS IN CHILDREN. REUEL E. BENSEN, M. Clin. North America **23**:661 (May) 1939.

It should always be remembered that gonorrheal vaginitis is not a venereal disease, although it is caused by the gonococcus. In almost every case it may be traced to a patient in the same family or hospital ward. Preventive measures directed to these sources of infection should always be instituted.

The acute stage is characterized by redness, swelling and edema of the labia, vagina and urethral orifice. The discharge may be evident or may be obtained only on passing a swab into the vaginal cavity. To obtain specimens of the discharge, the following method is useful: an ordinary glass catheter is inserted into physiologic solution of sodium chloride. A small amount remains in the catheter, which is then inserted as far as possible into the vagina. This is a painless procedure. The catheter is allowed to remain in position for a few seconds, and when it is withdrawn varying amounts of discharge will be found suspended in the solution. The character of the discharge is then determined by culture and by examination of thin smears on glass slides. A diagnosis based on smears alone is often misleading.

Vaginitis is always complicated by cervicitis. Infection is rarely found in the uterus or tubes. Ophthalmia rarely occurs in infants.

To check the spread of the disease a great deal of educational work with adults is necessary. Parents of patients should be thoroughly instructed in the prevention and care of the disease.

The general care of the patient with gonorrheal infection is important, and all measures necessary to increase her resistance should be encouraged. Ordinary local treatment is of doubtful value and is certainly harmful from a psychologic point of view. The routine use of estrogen in the form of vaginal suppositories is advised by Bensen. The same results may be obtained by hypodermic or oral administration or possibly by cutaneous inunction. The use of sulfanilamide is still in the experimental stage. EUGENE H. SMITH, Ogden, Utah.

OBSERVATIONS ON THE DESCENT OF THE TESTICLE WITH SPECIAL REFERENCE TO SPONTANEOUS DESCENT AT PUBERTY. R. E. SMITH, Arch. Dis. Childhood **14**: 1 (March) 1939.

Twenty-four boys with undescended testicles have been observed for from one to seven years. Spontaneous descent rarely occurred in those with associated hernias but did occur in a high proportion of the remaining 19 approximately at puberty, whether the testicle was unilaterally or bilaterally undescended. These testicles as judged by the usually accepted standards were thought to be functionally perfect. No harm results from postponing operation or gonadotropic therapy until puberty, at which time there is possibly an excess of natural production of gonadotropic hormone in circulation. Grave coincident disorders—torsion, tumor or inflammation—have not been noted. KELLY, Milwaukee.

RENAL DWARFISM. R. M. BATES, Brit. J. Child. Dis. **36**:34 (Jan.-March) 1939.

The case of a mentally defective woman who during life and at autopsy was thought to have renal rickets is described. Both kidneys showed pronounced nodular sclerosis and were greatly reduced in size. Examination of one femur showed no rachitic change, and the parathyroids were normal. LANGMANN, New York.

TORSION OF THE APPENDIX OF THE TESTIS. GEORGE D. F. MCFADDEN, Lancet **1**:320 (Feb. 11) 1939.

Torsion of the appendix of the testicle, or hydatid of Morgagni, is not well known. It is seen most commonly in children between 11 and 14 years of age; 1 of the author's patients was only 13 months of age.

Torsion of the testicle and torsion of the appendix of the testicle are the only two conditions that cause such rapidly increasing edema of the scrotal coverings. If the testicle hangs normally and the vas enters it in the normal relation, the diagnosis is torsion of the appendix and not torsion of the testicle. Treatment by surgical ablation of the appendix is described.

LANGMANN, New York.

TREATMENT OF THE INCOMPLETELY DESCENDED TESTIS. D. S. POOLE WILSON, Proc. Roy. Soc. Med. **32**:969 (June) 1939.

Under the age of 3 years the diagnosis of incompletely descended testis is uncertain.

The policy of awaiting spontaneous descent may be pursued until a boy is 10 years of age, but unless the testis lies in the superior scrotal position this policy should not be persisted in thereafter.

Glandular therapy may be employed before operative treatment as a means of determining whether the testes will descend spontaneously. It should be used only in the prepuberal period.

Operative treatment may be safely carried out at any age after 3 years and should be completed before puberty. The optimum period is between the ages of

8 and 11 years. The Bevan operation may be successful when the testis is very mobile, but the most consistent results are obtained by septal transposition or the Keetley-Torek operations. WILLIAMSON, New Orleans.

CASE OF GLOMERULONEPHRITIS ELEVEN YEARS AFTER DOUBLE EDEBOHL'S OPERATION. R. W. ILLINGWORTH, Proc. Roy. Soc. Med. **32**:1189 (July) 1939.

The case of a girl aged 19 years is reported. She first attended the hospital in 1927 because of puffiness of the feet and ankles. The progress notes from November 1927 to March 1929, with the results of special investigations, are given in the report. In March 1928 decapsulation of both kidneys was performed, and a year later the patient was discharged to a convalescent home with no edema. On reexamination eleven years later she was found to be well. There had been no relapses since her discharge from the hospital, and she was at work. WILLIAMSON, New Orleans.

DENDRITIC ADENOMA OF THE BREAST IN A GIRL 13 YEARS OLD. ANDRÉ MARTIN and JEANNE DELON, Bull. Soc. pédiat. de Paris **37**:22 (Jan.) 1939.

A girl 13 years old had a mass the size of an apricot in the left breast. It was excised. Histologically it had the structure of a papillary antracanalicular adenoma. When examined three years later the child was perfectly well. The opinion is expressed that if the tumor had not been removed it would have given rise to malignant epithelioma. BENJAMIN, Montreal, Canada.

ABNORMALITIES IN DESCENT OF THE TESTICLES. A. BELLEI, Lattante **10**:69 (Feb.) 1939.

Of 1,110 newborn infants, both full term and premature, 974 had both testicles in the scrotum and 136 (12.2 per cent) showed some abnormality in the descent of the testicles. Of the 136, 44 were premature infants; of the 974, 49 were premature infants. The incidence of abnormality was not proportional to the size of the full term child. In 83 per cent of the 136 cases the testes were in the inguinal canal. In 16 per cent one testis was in the scrotum.

Twelve of these infants were immediately given an estrogen by mouth; 5,000 units were given over a period of five weeks. No untoward results occurred; in 8 instances the testes had descended after five weeks of treatment; in 2, the testes had descended after two or three five week periods of treatment, and in the other 2 the testes had descended but had not yet reached the scrotum.

Failure of the testes to be in the scrotum of the newborn is probably an indication of a hormonal deficiency, perhaps only temporary, in the mother. The mother of the premature infant whose testes are descended has probably an abundance of hormone.

In conclusion, Bellei recommends that treatment of undescended testicles by estrogen be begun early and repeated at intervals in the unsuccessful cases. If the child reaches the age of 5 or 6 years and has not responded to several courses of glandular therapy, operation should be resorted to. HIGGINS, Boston.

NEPHROSIS IN INFANCY. A. WIEDERHOLD, Rev. chilena de pediat. **10**:465 (Aug.) 1939.

In the therapy of nephrosis in infancy, two essential points are important. Every possible infection must be guarded against on account of the low resistance of the infant organism.

In the treatment of ascites care must be taken to avoid pneumococcic or streptococcic infection. New methods for the relief of edema have caused the prognosis of infantile nephrosis to be more favorable. SCHLUTZ, Chicago.

Diseases of the Ductless Glands; Endocrinology

ENDOCRINE DISORDERS FROM A PUBLIC HEALTH ASPECT. J. H. HUTTON, Illinois M. J. **76**:78 (July) 1939.

Hutton points out that disorders of the endocrine glands are among the commonest of human disorders and that every physician is confronted by them, although he may not always recognize and properly treat them. The problem of recognizing endocrine disorders and treating them properly is one to be solved by the combined efforts of the health officer and the private practitioner.

The opportunity for the earliest recognition of endocrine disorders, of course, is among mothers and babies. The endocrine aspect of the problems involved should be given more attention by the workers in campaigns and clinics for maternal and infant welfare. The next important opportunity for recognizing abnormal endocrine conditions is among the school population. There the health officer may serve well by locating such disorders and referring them to the private physician. Hutton points out that the following signs of possible endocrine disorder should be looked for: abnormal tallness or shortness, obesity, abnormal genital development, abnormal hair growth and abnormal skin, nails or teeth, as well as failing scholarship and, perhaps, behavior problems.

BARBOUR, Peoria, Ill.

TONSILLECTOMY IN THE DIABETIC CHILD. A. H. TERRY JR., New York State J. Med. **39**:1622 (Aug. 15) 1939.

Ether is the anesthetic of choice. The operation should be done at midday, as this provides plenty of time to give the proper diet. The usual amount of insulin is given in the morning. The amount required later must be determined. Fluid should be forced, but no drugs are given before operation. The operation should take as little time as possible.

AIKMAN, Rochester, N. Y.

RELATIVE EFFICIENCY OF COMMERCIAL FORMS OF INSULIN. R. L. JACKSON and J. D. BOYD, Proc. Soc. Exper. Biol. & Med. **41**:15 (May) 1939.

A study of the diurnal blood sugar fluctuations in 12 well controlled diabetic children during treatment with regular insulin, protamine zinc insulin and zinc insulin crystals was made during one thousand and seventy-four days with 1,967 determinations of the blood sugar. When the insulin requirement did not exceed 1 unit per kilogram of body weight or a total of 20 units daily, single doses of protamine zinc insulin could maintain the blood sugar levels at approximately normal. It was not possible to stabilize the insulin requirement with protamine zinc insulin. It was possible to interchange regular insulin and zinc insulin crystals at will and repeatedly without altering the customary zone of diurnal blood sugar fluctuations.

HANSEN, Minneapolis.

NOTE ON PUBERAL GOITRE. J. C. SHEE, Irish J. M. Sc., November 1939, p. 802.

In a survey in a region of goiter, 27.67 per cent of children who were in the pubertal period had goiter. The author made a survey in a district where goiter was not endemic and found practically no goiter in 1,322 children. He states, accordingly, that the term "physiologic goiter" should not be used.

SNELLING, Toronto, Canada.

PATHOLOGIC CONDITIONS OF THE THYMUS GLAND IN INFANCY. A. CASTELLANOS, Arch. de med. inf. **8**:294 (Oct.-Dec.) 1939.

In Cuba there are a great number of children with symptoms of hypertrophy of the thymus. In many instances this condition has been diagnosed by plain roentgenograms, but such roentgenograms are not always to be relied on. Roent-

genograms of the anterior pneumomediastinum as developed by the author and Dr. Raul Pereiras give a definite diagnostic picture. By this means he believes that he has demonstrated that thymic hypertrophy can give rise to definite pathologic changes.

SANFORD, Chicago.

A POSSIBLE ETIOLOGIC RELATION BETWEEN THYMIC HYPERTROPHY AND SPRING CONJUNCTIVITIS. G. ALAMILLA, Arch. de med. inf. **8**:312 (Oct.-Dec.) 1939.

On the basis of a small number of cases, Alamilla believes that the thymus gland may be a factor in spring conjunctivitis. The fact that the thymus contains numbers of eosinophil cells speaks for its connection with allergic conditions. Further studies are being carried out.

SANFORD, Chicago.

VALUE OF CLINICAL AND ROENTGENOLOGIC DATA ON ACUTE CARDIAC INSUFFICIENCY IN THE INFANT. J. BONABA and M. L. SALDUN DE RODRIGUEZ, Bol. Inst. internac. am. de protec. a la infancia **13**:283 (Oct.) 1939.

There exists in some children a syndrome of primary acute cardiac insufficiency with cardiac dilatation. This syndrome is seen during the first part of infancy and less frequently during the second part. The clinical signs and symptoms are: sadness, depression, vomiting, spasmodic cough, dyspnea, cyanosis, cardiac enlargement, peripheral and internal edema, enlargement of the liver and ascites. There is no fever. This syndrome appears suddenly in eutrophic or dystrophic children, mainly in the first ones.

The evolution to healing comes in three ways: (*a*) complete healing with reintegration of the function and volume of the heart, (*b*) clinical healing with persistence of cardiac enlargement and (*c*) transitory healing with relapse.

The evolution to death is produced very rapidly, with the appearance in the last period of peripheral and internal edema and ascites.

The familial and personal antecedents do not permit one to draw any conclusion.

Treatment seems to have a decisive action. It should consist in depletive and cardiotenic therapy: phlebotomy and administration of digitalis and ouabain.

Pathologic examination shows a dilated heart without hypertrophy, malformation and valvular lesions, and congestion and cardiac edema of the internal organs. Histologically there is no change in the cardiac muscle.

The condition must be differentiated from bronchopneumonia, idiopathic hypertrophy and primary pericarditis.

FROM AUTHORS' SUMMARY.

NEUROBLASTOMA SYMPATHICUM OF THE RIGHT ADRENAL WITH METASTASES (HUTCHINSON TYPE). A. VON ALBERTINI and H. WILLI, Ann. pædiat. **152**:129 (Dec.) 1938.

In a case of neuroblastoma sympathicum of the adrenal, Hutchinson type, which had been well observed but not diagnosed clinically misleading findings in the blood picture and in the bone marrow were obtained. The first film of marrow from the tibia resembled leukosis on account of the preponderance of lymphoid tumor cells, while the blood picture showed a myeloid reaction. The second specimen of marrow, taken from the epiphysis of the femur shortly before death, corresponded to a reactive myeloerythroblastic marrow. The blood picture obtained at the same time pointed to leukemia on account of the abundant presence of lymphoid tumor cells. This change of the marrow picture taken together with the clinical aspect is characteristic for tumors of the bone marrow. The symptom complex and the differential diagnosis are freely discussed. The postmortem examination showed a neuroblastoma sympathicum originating from the right adrenal. The characteristic manner of the formation of secondary foci indicated the Hutchinson type. The tumor consisted of small lymphoid cells and presented

only occasional rosette forms, typical for this kind of neoplasm. Apart from this tumor, a ripe ganglioneuroma was found in the right adrenal. This means a collection of tumors of the same histiogenic class in different stages of development, originating in the same organ. FROM AUTHORS' SUMMARY.

ADRENAL FUNCTION AND VITAMIN C. K. CHOREMIS, E. PAPACHRISTOU and J. KORKAS, Ann. pædiat. **154**:22 (Oct.) 1939.

During grave toxic infectious diseases in which physiologic research detects changes in the adrenals, the epinephrine hyperglycemia does not become apparent and the blood sugar curve is flattened. Epinephrine hyperglycemia reappears if the epinephrine function is helped by the administration of vitamin C and extract of adrenal cortex. In grave conditions—septicemia, for example—the efficacy of epinephrine ceases completely and reactivation by vitamin C and extract of adrenal cortex becomes impossible. The authors are of the opinion that in the first case the adrenals have suffered only functional damage, while in the latter case a severe anatomic lesion has to be assumed.

The enhancement of the function of epinephrine by vitamin C is the result of the improvement of the function of the cortex. It is annulled if cortical function becomes inert through a salt-free diet. In that case vitamin C and extract of adrenal cortex assume the properties of insulin. This interesting observation shows that sodium chloride represents a necessary factor for the regulation of the effect of vitamin C, extract of adrenal cortex and epinephrine on sugar metabolism. It results from the foregoing facts that the presence of vitamin C is necessary for the physiologic functioning of extract of adrenal cortex. This also explains the fact that a fair amount of vitamin C is found in the adrenal cortex.

Vitamin C by itself cannot exert an influence on the acid-base balance, only vitamin C combined with extract of adrenal cortex and the latter alone. Extract of adrenal cortex causes a marked shift of the acid-base balance toward the alkaline side. Vitamin C and extract of adrenal cortex prevented the lowering of the alkali reserve and were able to shift the chemical properties of the blood toward the alkaline side. Thus they have a checking effect on the acidotic property of epinephrine.

Vitamin C and cortical substance are alternately correlated, i. e., reduction of vitamin C eliminates the effect of cortical substance, and hypofunction of cortical substance favors the rise of scorbutic manifestations. Thus functional or anatomic disturbance of the adrenals produces weakening of the vitamin action; alternatively deficiency of vitamin C of any origin will create weakening or destruction of the adrenals' functional efficacy. The authors' investigations prove indeed that diseases which demand a large consumption of vitamin C—for example, tuberculosis and typhoid—frequently exhibit disturbances of cortex function. The metabolic changes resulting from these conditions show a uniform course, the terminal form of which is presented by Addison's disease and scurvy. These terminal forms of adrenal insufficiency or avitaminosis are, however, preceded by many deviations from the physiologic which, as mentioned, can be ascertained by biologic experiments.

Thus it is proved that the organism long before it reaches those ultimate phases when it has not only used up all its stores of vitamin C but also exhausted all the different regulatory possibilities, exhibits pathophysiologic changes as signs of incipient derailment of the metabolism. It is, even under physiologic conditions, of course, not easy to find the beginning of these alternate actions, whether the vitamin deficiency comes first and the change of cortex function follows, or vice versa. Under pathologic conditions it is even less possible to ascertain the primary lesion. In spite of this the authors believe that the therapeutic use of the drugs mentioned does not lose in importance under such pathologic conditions, a belief which is confirmed by their practical experience. FROM AUTHORS' SUMMARY.

DIABETES INSIPIDUS. H. BERNHARDT, Med. Klin. **35**:143 (Feb. 3) 1939.

Diabetes insipidus is one of the most reliable manifestations to be observed in the diagnosis of disorders of the hypophysial system, or midbrain, which is of great importance in vegetative regulations. For the diagnosis of latent diabetes insipidus it is necessary to: (1) determine the daily fluid intake and output, (2) perform a urine concentration test and (3) make studies of the blood. Treatment is mainly symptomatic, with hypophysial extract (preferably in powdered form intranasally). The diet should be low in salt, and fluids should be restricted. In some cases short wave therapy to the hypophysial region is apparently beneficial.

SIEMSEN, Chicago.

Diseases of Muscles, Bones, Joints and Lymph Glands

STUDIES IN DYSTROPHIA MYOTONICA: I. HEREDITARY ASPECTS. A. RAVIN and J. J. WARING, Am. J. M. Sc. **197**:593 (May) 1939.

Ravin and Waring present four family trees in which the disease occurred. In these family trees, among 33 members examined 12 were found to have dystrophia myotonica.

A table is presented in which most of the instances of direct transmission of the disease from parent to child which have been recorded in the literature are tabulated. This table shows strikingly that in all of these cases the onset of the disease in the children was at a definitely earlier age than the onset in the parents.

Evidence leads to the conclusion that dystrophia myotonica is transmitted as a single factor dominant but that this dominance is modified by "progressive inheritance." In "progressive inheritance" the onset of the disease is at an earlier age in each succeeding generation, and the disease increases in severity in succeeding generations.

Because of the presence of progressive inheritance, on the one hand, the parents of many patients may show little or no sign of the disease, and, on the other hand, the children of patients tend to present the disease so early as to prevent further propagation, and the disease dies out in the family.

Possible changes in the germinal material which could produce this type of heredity are described.

EMKE, Omaha.

A STATISTICAL STUDY OF ALLERGY IN ARTHRITIS. E. F. TROUT and E. G. VRTIAK, Ann. Int. Med. **13**:761 (Nov.) 1939.

Allergy occurs more frequently and is of greater severity in rheumatic patients than in controls.

READING, Galveston, Texas.

QUININE AND DYSTONIA MUSCULORUM DEFORMANS. G. B. HASSIN, J. A. M. A. **113**:12 (July 1) 1939.

An 8 year old girl is described among 3 patients afflicted with dystonia musculorum deformans who were benefited by the administration of quinine in a manner similar to that in cases of myotonia congenita of Thomson. Untreated, she exhibited marked distortion of posture, especially late in the day. There were jumpy movements of the extremities and neck. After treatment there remained only some dragging of the feet in walking.

HEERSMA, Kalamazoo, Mich.

HEREDITARY OSTEOCHONDRODYSTROPHIA DEFORMANS. A. W. JACOBSEN, J. A. M. A. **113**:121 (July 8) 1939.

The clinical and roentgen findings of this disease in two brothers, a cousin and the grandfather are presented. These patients belonged to a family in which 20 members were affected in five generations. Jacobsen discusses the hereditary factor in this and other types of rare bony and cartilaginous maldevelopment.

HEERSMA, Kalamazoo, Mich.

DIFFERENTIAL DIAGNOSIS OF NONRHEUMATIC "GROWING PAINS" AND SUBACUTE RHEUMATIC FEVER. M. J. SHAPIRO, J. Pediat. **14**:315 (March) 1939.

Shapiro reviews the literature dealing with the significance of "growing pains" and presents his own point of view. He believes that there is a distinct clinical difference between nonrheumatic growing pains and subacute rheumatic fever, that growing pains are not due to the rheumatic infection and that in children with such pains rheumatic heart disease does not develop. Virtually all patients with rheumatic heart disease, especially children and young adults, give a positive history of rheumatic infection. Nonrheumatic growing pains occur early in childhood and may continue through adolescence, and they do not as a rule follow infections of the upper respiratory tract. These pains occur usually at the end of the day, sometimes during the night, and are gone by morning. The pains are localized most commonly in the muscles of the legs and thighs, rarely in the muscles of the upper extremity, and only occasionally in the knee joints. No other rheumatic symptoms occur as a rule, no objective signs are present and all laboratory observations are normal.

RAUH, Cincinnati.

OSTEOMYELITIS IN CHILDREN. A. R. SHANDS JR., Nebraska M. J. **24**:361 (Oct.) 1939.

Osteomyelitis is most common in children between the ages of 3 and 16 years. In one large series of patients 91 per cent were under 20 years. The disease is four times as common in boys as in girls, and the lower extremities are more often affected than the upper. In 95 per cent of the patients the osteomyelitis is in the long bones, in this order of frequency: the tibia, the femur, the humerus and the radius. The staphylococcus is the infecting organism in approximately 90 per cent of the patients. The infection is usually borne by the blood. The portal of entry for the staphylococcus is most frequently the skin; for the streptococcus it may be the tonsils, the teeth or the sinuses. The onset of osteomyelitis is sudden, with pain, fever, chills and prostration. Roentgen examination is of little value in diagnosing early acute osteomyelitis. The disease must be differentiated from arthritis, rheumatism, cellulitis, thrombophlebitis, erysipelas, scurvy and infantile paralysis. The statement is made that the mortality in children under 2 years of age has decreased from 50 to 5 per cent since the disease has ceased to be considered a surgical emergency and the patient is considered rather than the disease. Conservatism is distinctly the keynote in treatment, and too great haste in operation is not advised. Staphylococcus and streptococcus antitoxin may be of great value. Sulfanilamide, gentian violet and mercurochrome may be of value. Extensive removal of the bone early is contraindicated, and a sequestrectomy may be done later. The Orr method is indicated later. Maggots have been found useful.

HAMILTON, Omaha.

ACUTE OSTEOMYELITIS. C. T. HARRIS, New York State J. Med. **39**:1554 (Aug. 15) 1939.

Thirty-six children with acute osteomyelitis have been seen in the Strong Memorial Hospital in a period of ten years; 2 of these were less than 2 years of age, and 19 were between the ages of 2 and 12 years. Seven of the 36 children died. Cultures of material from wounds showed Staphylococcus aureus in 29 cases.

The patients were treated by many methods and by various surgeons and orthopedists. Forty-four per cent of them had symptoms dating back from two to seven days before admission. Early diagnosis is again urged. Acute pain near the epiphysis, coming on suddenly in an otherwise well child, with a sharp rise in temperature, is always suggestive of osteomyelitis. While one is waiting for positive roentgen evidence, for complete laboratory studies or positive cultures, the ideal time for early surgical intervention may pass.

AIKMAN, Rochester, N. Y.

CHONDROMYXOSARCOMA AND OSTEOCHONDROSARCOMA. L. E. SORRELL, South. M. J. **32**:1046 (Oct.) 1939.

In 2 cases of chondromyxosarcoma the lesions were near the knee. An enlargement or painful growth anywhere on the body is a dangerous symptom. It is of great importance that an immediate diagnosis be made and treatment given.

SCHLUTZ, Chicago.

VASCULAR ANOMALIES OF UPPER LIMBS ASSOCIATED WITH CERVICAL RIBS. R. M. HILL, Brit. J. Surg. **27**:100 (July) 1939.

Hill cites a case of bilateral cervical ribs accompanied only with vasomotor disturbances of the hands of the acrocyanotic type in which removal of a rib and the fibromuscular band relieved pain, diminished swelling and improved the color of the hand on the corresponding side. Other anatomic variations are worthy of consideration in cases of vascular disorders of the upper extremities, and with rational indications exploratory operation in this region would be warranted.

J. A. M. A.

CONGENITAL MYOTONIA IN THE GOAT. G. L. BROWN and A. M. HARVEY, J. Physiol. **96**:11P, 1939.

Brown and Harvey studied a strain of goats with congenital myotonia. They observed the effects of electrical stimulation of the nerve fibers and of acetylcholine on the voluntary muscles. They conclude that the abnormality is in the muscle fibers and not in the neuromuscular transmitting apparatus.

THOMAS, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

SWELLINGS AND SINUSES IN THE NECK IN CHILDHOOD. C. DONALD, Practitioner **144**:66 (Jan.) 1940.

Involvements of the structures of the neck are common in childhood. The great majority are inflammations of the lymph glands, and these inflammations are often tuberculous. There are also congenital cysts and sinuses, neoplastic formations and occasional thyroid swellings. The most serious of these various conditions are lymphosarcoma, lymphadenoma and acute simple infectious inflammations, such as streptococcic lymphadenitis or Ludwig's angina. But swellings, however trivial, in the neck are a great worry to parents, more so than those in other regions. The reasons are not far to seek. The lesion is ever obvious and the possibility of operation and anesthesia ever present. Parents dislike being separated from their children. Still illness and ill timed incisions leave scars which are a reproach to the medical profession. Accordingly, an early, highly accurate diagnosis and a reasonable outline as to the probable future course and possibilities are much to be commended.

GELSTON, San Francisco.

ALBERS-SCHÖNBERG DISEASE IN A NEWBORN INFANT. N. I. HEYBROEK, Maandschr. v. kindergeneesk. **8**:415 (July) 1939.

A newborn baby was found to have Albers-Schönberg disease. The blood showed marked erythroblastemia and thrombopenia and a number of myelocytic elements. After nine days the child died with symptoms of hemorrhages and fever. The autopsy showed general increased density of the bones, with modification of the bone marrow, and leptomeningitis. The bone marrow showed large pale polygonal cells without hemopoietic cell tissue. The vertebrae had the typical form of a diabolo. The author is of the opinion that the fetal form of Albers-Schönberg disease is an alteration of the mesenchyma taking place during the second month of fetal life.

VAN CREVELD, Amsterdam, Netherlands.

CALCINOSIS INTERVERTEBRALIS. J. L. KEYZER, Maandschr. v. kindergeneesk. **8**:467 (Sept.) 1939.

A boy of 2½ years came into the hospital with a high fever and severe pains in the neck, which prevented sleep; he showed no evidence of meningitis. Roentgen examination disclosed calcification in three intervertebral disks of the neck. A stretching apparatus was applied to widen the spaces between the cervical vertebrae, with favorable results; however, the chalky shadows remained. The diagnosis was chondritis intervertebralis acuta infectiosa calcarea (calcinosis intervertebralis). A blood culture showed a growth of weakly hemolytic streptococci, which most probably played a role in the inflammatory process that preceded the calcification.

VAN CREVELD, Amsterdam, Netherlands.

RENAL OSTEOPOROSIS. S. VAN CREVELD, Nederl. tijdschr. v. geneesk. **83**:1923 (April 29) 1939.

In this clinical lecture the combination of chronic renal disease and severe osteoporosis observed in a young girl is discussed. In regard to clinical course and deviation of metabolism, this case is compared with typical cases of renal rickets, on one hand, and with cases in which the so-called syndrome of Debré–de Toni–Fanconi is prominent, on the other. The significance and the extension of the problem of renal osteoporosis in recent years are discussed in general.

FROM AUTHOR'S SUMMARY.

Diseases of the Eye

CONGENITAL BILATERAL ANOPHTHALMOS. JOSEPH SCHWARTZMAN and ANTHONY MAFFIA, Arch. Pediat. **56**:240 (April) 1939.

A case of congenital bilateral anophthalmos with cleft palate and polydactylism is reported. Heredity has been demonstrated often enough to indicate a recessive familial factor as basic.

Since deleterious factors during embryonic development appear to play some part in production of the condition, it is essential that careful, early and frequent prenatal attention be given in all cases to detect and remedy as soon as possible all illnesses and abnormalities so as to limit their effects to the minimum. Once the condition is present, there is no treatment except plastic surgical procedures.

ORR, Buffalo.

HEREDITARY AND FAMILIAL MEGALOCORNEA. P. BEIL and L. SARRAZIN, Ann. d'ocul. **176**:241 (April) 1939.

Cases of this curious affliction, although rare, are important. Mayer in 1808 in a thesis alluded to familial deformities of the cornea, but it was Horner who first studied the question.

Megalocornea is a domelike deformity of the cornea appearing at birth. The cornea is otherwise regular and clear, only the limbus presenting a characteristic opacity. The vertical and horizontal diameters range between 12 and 16 mm. The normal curve is variable, and generally there is astigmatism. The visual clearness is frequently normal. The expansion of the anterior segment is striking, and the anterior chamber is enlarged in all its dimensions. Iridodonesis is nearly always present, and the lens does not follow the enlargement of the anterior segment but remains normal in volume.

For many years this ocular malformation is compatible with good sight. It may not affect the patient's vision until between the fortieth and the fiftieth year, when bilateral cataract appears, frequently associated with dislocation of the lens.

Three patients, two brothers and a cousin, were seen by the writer, and the details of the examination are given. Concerning the treatment of this condition and the results obtained, Weil, of Strasbourg, reported cases in which operation was successful. He noted, as did Horner, that the lens keeps a normal volume and does not follow the anterior chamber in its hypertrophy.

Four illustrations and a bibliography accompany the article.

S. H. McKee [Arch. Ophth.]

Origin and Treatment of Strabismus. H. Schmelzer, Med. Klin. **35**:629 (May 12) 1939.

Schmelzer discusses the types and causes of strabismus. Convergent strabismus is the most common. In about one half of the patients it occurs at the age of 2 to 3 years, frequently in connection with a disease of childhood. Early treatment is imperative; it involves correction of refractive errors with glasses and training of the eye with defective vision while the good eye is covered. Covering of the good eye should not be continued too long, as the vision may deteriorate. If there are anomalies of the ocular muscles, surgical alterations are necessary. Since some correction occurs with growth, the extent of the operation is problematic. The time for operation is also problematic. The author favors the age of 10 years. The functional result is more important than the cosmetic result. Postoperative stereoscopic exercises are important.

External strabismus is much less frequent (about 1 to 5); operative treatment is usually necessary.

Strabismus associated with diplopia in later childhood usually denotes cerebral disturbance.

Siemsen, Chicago.

Skin Diseases; Allergy

Oral Ragweed Pollen Therapy. M. Zeller, J. Allergy **10**:579 (Sept.) 1939.

Zeller concludes from his experiments that enteral absorption of ragweed pollen was not demonstrated by passive transfer and direct skin tests. He therefore sees no advantage in oral therapy and feels that the best results are obtained by the hypodermic method. However, among those who discussed his paper were some who still held hope for oral therapy. They contended that the fact that some persons manifest constitutional symptoms following ingestion of pollen extract and the fact that a proteose has been demonstrated in the urine of patients who ingested pollen extract cannot be disregarded.

Hoyer, Cincinnati.

Epinephrine in Oil: Its Effect in the Symptomatic Treatment of Hay Fever. E. L. Keeney, J. Allergy **10**:590 (Sept.) 1939.

Injections of 0.2 to 0.5 cc. of epinephrine in oil were given to 35 adults who had hay fever. Relief of symptoms varying from 25 to 100 per cent was obtained in 30 of the 35 patients. The effect lasted twelve to thirty-six hours. A few of the patients experienced nervousness for one to three hours. This experience was prevented subsequently by reducing the dose.

Hoyer, Cincinnati.

Prophylaxis and Treatment of Poison Ivy Dermatitis with an Extract of Rhus Toxicodendron. L. Zisserman and L. Birch, J. Allergy **10**:596 (Sept.) 1939.

The experiment was carried out at a camp conducted by the Philadelphia Boy Scouts' Council. A total of 1,731 boys were studied; 304 received prophylactic injections of a 1:1,000 dilution of the antigen in olive oil. The dose received

varied from 0.25 to 0.5 cc., followed a week later with 1 cc. From the tables given, the results indicate that the two injections made the subject more susceptible to rhus dermatitis. Especially was this true of those who were susceptible to the disease.

HOYER, Cincinnati.

TREATMENT OF INFECTIONAL ASTHMA IN CHILDREN WITH FILTRATES OF CULTURES OF UPPER RESPIRATORY PATHOGENIC BACTERIA. F. A. STEVENS, J. Pediat. **14**:307 (March) 1939.

Fifty-three children with infectional asthma were treated with gradually increasing doses of filtrates of cultures of the common pathogenic bacteria of the upper respiratory tract. Filtrates of cultures of bacteria found in the respiratory tract were prepared, and to them were added filtrates of other pathogens not found when the cultures were made. This combination of filtrates was used because the bacterial flora of the respiratory tract was found to vary in each attack of asthma and the cutaneous reactions to the nucleoproteins of these bacteria were found to change constantly. Of the 53 children who received persistent treatment with these filtrates, 50 are apparently well; 12 have been symptom-free during their second or third year of treatment and will require no further treatment; 32 have been symptom-free from one to four years without treatment, and 6 have been well for more than four years.

RAUH, Cincinnati.

ACRODYNIA. H. M. JAHR and R. C. DORNBERGER, Nebraska M. J. **24**:391 (Oct.) 1939.

Typical acrodynia was observed in a child of 3 years. Jahr and Dornberger stress the use of vitamins and the elimination of any foci of infection. This child was given nicotinic acid.

HAMILTON, Omaha.

RENAL LESIONS IN CHILDREN WITH ERYTHEMA NODOSUM. A. WALLGREN, Arch. Dis. Childhood **14**:271 (Sept.) 1939.

During the toxic-allergic-febrile state induced by various infections, in which erythema nodosum appears, there is frequently present evidence of renal lesions. These are usually subclinical but may manifest themselves as acute hemorrhagic nephritis. They are probably to be regarded as an expression of the same toxic or allergic remote action of the infectious agent that produced the eruption of erythema nodosum and the capillary fragility of the skin.

KELLY, Milwaukee.

THE SEBORRHOEIC DIATHESIS. J. T. INGRAM, Brit. M. J. **3**:5 (July 1) 1939.

This special paper is summarized as follows:

"It is suggested that the problems of seborrhoeic disorders are related to and dependent upon the seborrhoeic diathesis and not to any great extent upon seborrhoeic or other organisms.

"The disturbances of physiological function characteristic of the diathesis are manifest particularly in the membranes of the upper respiratory and gastro-intestinal tracts as well as the skin. As a consequence seborrhoeic patients are subject to chronic infection of the upper respiratory tract and to dyspepsia and malnutrition.

"These conditions, together with the underlying nervous and temperamental instability, have an important bearing on aetiology and treatment."

ROYSTER, University, Va.

XERODERMA PIGMENTOSUM. G. H. PERCIVAL, Tr. Med.-Chir. Soc., Edinburgh, 1939, p. 114; in Edinburgh M. J., August 1939.

Two cases of xeroderma pigmentosum are presented by Percival, who describes the condition as rare, only 2 other cases being known in Edinburgh and only a dozen cases recorded in all of Scotland. When the disease begins the patient is usually about 2 years of age, at which time there appears an undue sensitivity to sunlight, the child staying sunburned at the end of summer. Some patients wear a veil to protect themselves from the sunlight. The pigmentation, freckling, erythema and areas of telangiectasis are similar to the effects from roentgen exposure. Finally, when the child is about 5 years of age, the skin begins to show warty growths, which enlarge and undergo cancerous degeneration. If neglected, glandular involvement follows and the patient dies.

In the first case some improvement occurred from roentgen treatment, but the prognosis was still unfavorable. In the second case the roentgen ray appeared to produce a better effect than radium.

NEFF, Kansas City, Mo.

DIGITAL MUTILATIONS IN INFANTILE ACRODYNIA. F. GADRAT, J. LASSERRE and R. PETEL, Arch. de méd. d. enf. **12**:559 (Sept.) 1939.

Juvenile acrodynia, the identification of which has been established only within recent years, is by many considered a relatively benign condition. Reports from many countries, however, demonstrate that this opinion is incorrect; visceral complications and intercurrent disease may readily transform the disease into one of high malignancy. Ulcerogangrenous involvement of the extremities constitutes one of the most formidable among the complications of acrodynia in young subjects. This major invasion was discussed by Parkes Weber, R. Debré and Mlle. Pétot, Caussade and others, who published the earliest observations on acrodynia. The present authors report 2 additional cases, in which gangrene affected the fingers and hands of a girl 23 months of age and a girl 3 years of age. The former recovered with severe mutilations, while the latter died of exhaustion after an illness of three months. Complete histologic reports complete the clinical studies.

AMESSE, Denver.

RECKLINGHAUSEN'S DISEASE IN CHILDREN. A. CARRAU and A. P. DE SANTIAGO, Arch. de pediat. d. Uruguay **10**:289 (May) 1939.

Three children with Recklinghausen's disease showed the cardinal symptoms, namely, generalized neurofibromatosis, cutaneous pigmentation, superficial skin tumors disseminated all over the body, tumors of the nerves and somatic changes. In 1 patient dysfunction of the hypophysis was an associated symptom and predominated. This patient had pronounced symptoms of the dystrophia adiposogenital syndrome, with marked physical changes. In another patient there were marked bony changes of the thorax.

SCHLUTZ, Chicago.

CAUSES OF ACRODYNIA IN CHILDHOOD. R. DEBRÉ and A. NÉVOT, Ann. pædiat. **152**:253 (Feb.) 1939.

Debré and Névot call to mind that ever since 1927 Debré has tried to establish that ergotism, ustilaginism, infantile acrodynia (pink disease) and pellagra belong to the same nosologic group. This view is confirmed by more recent papers, among them one by Mayerhofer and Dragisic, which appeared in July 1938. If one recognizes that alimentary intoxication is the origin of ergotism and ustilaginism, it is difficult to ascribe a different origin to acrodynia and pellagra, although alimentary intoxication is not definitely proved to be the cause of the latter conditions.

The authors show experimentally that disturbances similar to the aforementioned ones (vasomotor, trophic and paralytic disorders and death) can be produced in

animals by feeding them extracts of ergot, of collar bags (Ustilago segetum), of brown rust (Tilletia tritici) and of the seeds of corn cockles. It is necessary to remember particularly the variable but undeniable toxicity in animals used for experimental purposes of the spores of brown rust of wheat, contained frequently in human food, also of the seeds of corn cockles and of blight of wheat, which are much more rarely ingested. Numerous epidemologic investigations undertaken by the authors in various parts of France failed to establish that in the regions where acrodynia was prevalent such a food was taken by children or was present in cows' fodder.

However, this problem remains, and in order to ascertain the causes of acrodynia and to determine whether the theory of an origin in alimentary intoxication is right it is necessary to study carefully the dietary regimen of the child and the possible parasitic infestation of his food, including the milk, which may contain toxic substances of a vegetable origin. FROM AUTHORS' SUMMARY.

SCLERODERMA AND CALCINOSIS. O. SAXL, Ann. pædiat. **154**:103 (Nov.) 1939.

Severe diphtheria in a 9 year old girl was followed by serious postdiphtheria complications. At the end of the second month, the first changes in the skin appeared. By degrees scleroderma and calcinosis developed. The process was combined with an increase in the lime content of the blood and a negative calcium balance. After two years and three months, there occurred sudden aggravation, following angina. Therefore the parathyroid glands were partially removed, and it was found that the upper left one had enlarged in a tumor-like fashion. In spite of the operation the child's condition became worse, and she died two weeks later.

Scleroderma is considered an illness of the whole connective tissue depending on a toxic, septic or allergic injury to the blood vessels. The disturbance of the internal secretion is to be explained partially by a damage of the connective tissue injuring subsequently the parenchyma; partially it may be caused by direct irritation of the parenchyma. Saxl administers opotherapy where signs of disturbance of one gland are predominant. Surgical intervention when strictly indicated may also meet with success; otherwise one may succeed only by finding the point of invasion and by isolating it carefully. FROM AUTHOR'S SUMMARY.

Surgery and Orthopedics

CONSERVATIVE TREATMENT OF CONGENITAL CLUB FEET IN INFANTS. L. S. SELL, South. M. J. **32**:1199 (Dec.) 1939.

Sell believes that a method of treatment in which a series of plaster casts and wedgings is used without use of an anesthetic and without forcible manipulations and operations is of great value.

No originality is claimed either for the method or for the principles described, but it is hoped that the advantages of the conservative method will be appreciated and widely adopted by surgeons dealing with clubfoot. SCHLUTZ, Chicago.

THE THREE-DYE TREATMENT OF BURNS. J. B. DEVINE, M. J. Australia **1**:924 (June 24) 1939.

The advantages of treating burns by the three dye method (1 per cent aqueous solution of gentian violet, 1 per cent aqueous solution of brilliant green and a 0.1 per cent solution of neutral acriflavine) are as follows: 1. The mixture is inexpensive and keeps indefinitely. 2. The mixture forms a coagulum rapidly and with only one or two applications, and the coagulum is more pliable than that of tannic acid. 3. The analgesic action of the gentian violet relieves pain very

rapidly, and the mixture is powerfully antiseptic and more efficient in preventing infection than tannic acid.

The disadvantages of the method are: 1. The mixture stains clothing and linen. 2. In very small children and babies the coagulum formed may be too thick and may crack at the edges.

GONCE JR., Madison, Wis.

CONGENITAL ANODONTIA WITH ABNORMALITIES OF THE DERMAL SYSTEM (ECTODERMAL IMPERFECTION), WITH REPORT OF A CASE. R. RINVIK and A. SYRRIST, Acta pædiat. **23**:548, 1939.

A 5 year old boy exhibited not only absence of teeth but, roentgenographically, a lack of all dental rudiments save one bud. In addition, he showed many of the features characteristic of hereditary ectodermal dysplasia: specifically, saddle nose, ozena, a sparse growth of lanugo-like hair and absence of sweat glands and sebaceous glands. Mental development was retarded. Approximately 6 cases of this sort have been reported in the literature. The cause, which is doubtless genetic, and the genesis are discussed. The bibliography is useful.

MCCUNE, New York.

Miscellaneous

CASE OF OIL OF CHENOPODIUM POISONING: TREATMENT WITH FORCED PERIVASCULAR (SPINAL) DRAINAGE. T. L. BIRNBERG and C. L. STEINBERG, Arch. Pediat. **56**:304 (May) 1939.

The dangers of poisoning from oil of chenopodium are discussed, and it is noted that severe cerebral involvement is not uncommon. In the case reported, a 2½ year old girl ingested 72 minims (4.5 cc.) of the oil in a period of ten days. Rapid clinical response followed forced perivascular drainage.

ORR, Buffalo.

STUDIES ON THE MODE OF ACTION OF SULFANILAMIDE IN VITRO. J. T. WELD and L. C. MITCHELL, J. Bact. **38**:335 (Sept.) 1939.

The authors believe that their experiments dealing with the effect of sulfanilamide on the growth of the streptococcus in rabbit serum reveal interesting facts. Sulfanilamide in moderate concentrations is bactericidal only for streptococci which are multiplying relatively slowly. The bactericidal action of sulfanilamide appears to be increased when the organisms are grown at elevated temperatures. The experiments do not seem to support the theory that sulfanilamide interferes with the power of streptococci to utilize serum proteins or that peptone per se interferes specifically with the bactericidal effectiveness of sulfanilamide.

STOESSER, Minneapolis.

PREGNANCY IN CHILDHOOD. H. VIGNES and R. HAMELIN, Presse méd. **47**:1257 (Aug. 16) 1939.

Vignes and Hamelin have compiled statistics concerning the course of pregnancy occurring in childhood. In France 1 in 1,653 pregnancies occurs before the age of 15. Usually precocious pregnancy follows precocious puberty. The frequency of pregnancy during the first year of marriage is shown to drop sharply as the age increases. Although the subjects of precocious pregnancy are usually physically and sexually advanced for their age, there have been examples of pregnancy before loss of the first teeth. Numerous cases have been reported in which menstruation had not been established at the time of pregnancy. The complications of pregnancy occur in about the same frequency in these children. Premature

labor is more common. Surprisingly enough, labor itself is usually not difficult, and normal delivery is the rule; 97 per cent spontaneous deliveries are reported. Lactation is possible, and 1 case is cited of a 6½ year old mother who nursed her child nine months. The babies tend to be male but weigh less than the average. Although pregnancies occurring late in adolescence are not dangerous, pregnancy occurring in childhood definitely has its dangers.

DAFFINEE, Boston.

RESEARCHES TO DETERMINE THE OPSONIC AND COMPLEMENTARY POWER OF BLOOD SERUM. THE BACTERICIDAL POWER OF WHOLE BLOOD AND THE SEDIMENTATION RATE OF THE RED BLOOD CELLS IN EXPERIMENTAL INTOXICATION FROM THALLIUM. B. VASILE, G. GRANOZZI and F. PECORELLA, Pediatria **45**:322 (April) 1937.

Vasile, together with two assistants, has made an experimental investigation of the complementary and opsonic power of the blood serum, of the bactericidal power of the whole blood and of the sedimentation rate of the red blood cells in children subjected to the administration of thallium in therapeutic doses and in rabbits intoxicated with the same metal.

In the case of the children the authors observed that after the administration of the drug the opsonic and complementary powers of the blood serum, as well as the sedimentation rate of the red blood cells, increase, while the bactericidal power of the whole blood shows no change.

For the purpose of revealing the mechanism by which thallium brings about these changes in the indexes of immunity, the authors have performed a series of experiments on the eventual influence of thallium in vitro on these same indexes. By this means they have been able to exclude any direct influence of the metal. They believe that there is an endocrine factor which when activated by the metal causes the aforementioned changes; they especially implicate the thyroid, the function of which becomes greatly stimulated by therapeutic doses of the metal and depressed by toxic doses.

These facts have been observed and studied in rabbits without thyroid glands and in those overdosed with thallium. Here there has been a marked change in the indexes of immunity.

PALMIERI, Brooklyn.

MORPHINE SUSCEPTIBILITY IN INFANCY. U. GRUNINGER, I. GRABY and A. C. OHLING, Monatschr. f. Kinderh. **79**:169 (Aug.) 1939.

In a clinical study the writers confirmed observations which have shown that morphine can be offered with reasonable safety to infants. It must be used with great care in those under 4 months of age. They found, however, that a dose of 0.02 mg. per kilogram of body weight had no effect on the frequency of respiration.

GERSTLEY, Chicago.

RESEARCHES DEALING WITH TWINS; THEIR RELATION TO PEDIATRICS. T. BRANDER, Acta pædiat. **21**:5, 1937.

The abstracter does not pretend to have read with the attention that it merits this 132 page monograph in which is condensed and digested material derived from an examination of a literature which the author describes as fathomless; in support of this characterization the author adduces a bibliography of approximately 540 titles. The methodology of human genetics is outlined. Then follows an account of the historical and technical aspects of researches into human twinning: The author calls attention to certain problems of pediatric interest the solution of which can best be approached through this type of study. He expresses regret that in pediatric circles this method of investigation has not received the attention that it deserves, pointing out that copious and valuable

case material is lost through lack of proper identification. The plea is voiced that every hospital and clinical record of a twin be distinguished by a suitable label so that it may easily be recalled for subsequent survey.

McCUNE, New York.

DOSAGE OF PILOCARPINE FOR CHILDREN. E. SELESTE, Acta paediat. **21**:401, 1937.

Clinical observations on 22 children varying in age from 2½ months to 10 years and 8 months and in weight from 3.5 to 32.9 Kg. demonstrate that the maximal tolerable dose of pilocarpine given by mouth to patients 1 year or older varied between 10 and 30 mg. (average, 1.005 mg. per kilogram of body weight), and to infants under 1 year, between 2 and 10 mg. (average, 1.4 mg. per kilogram). The tolerable hypodermic dose was much smaller.

McCUNE, New York.

Society Transactions

CHICAGO PEDIATRIC SOCIETY

GERARD N. KROST, M.D., *President*

GEORGE F. MUNNS, M.D., *Secretary*

Regular Meeting, April 16, 1940

Control of the Common Contagious Diseases Within a Children's Hospital. DR. HOWARD M. JACOBS and DR. MAURICE L. BLATT.

One of the important problems in the administration of a children's hospital is the prevention of cross infection with the common contagious diseases of childhood. In order to control such cross infection a definite plan of administration and organization has been in effect in the children's division of the Cook County Hospital for the past ten years. The children's division has continued to serve the community without interruption from quarantine during this period.

(Charts were shown by Dr. Jacobs outlining the principles and procedures used.)

The receiving department of the Cook County Children's Hospital is so constructed that contact between patients applying for admission is unavoidable. There is no cubicle space available for children awaiting examination. Patients wait on a common bench. Since it is impossible to avoid such contacts in the receiving department, a preliminary sorting of patients is made by routing all children above 2 years of age through the main examining room. The main examining room also has a common waiting room.

Children under 2 years of age come directly to the receiving department of the children's building, not because they are less frequently bearers of contagion but to give them the benefit of an immediate primary examination by a trained pediatric personnel.

In spite of the most careful sorting and isolation by the receiving department, patients are nevertheless admitted to the wards from time to time in the incubation period of a contagious disease. The careful management of such patients is of importance in preventing an epidemic.

When a contagious disease is suspected in a child after admission to the ward, isolation nursing care for the patient and his contacts is instituted at once. As soon as a definite diagnosis has been made, the child is transferred to the contagious division and his contacts are placed under quarantine. One cardinal principle always followed is that a patient with a contagious disease is never moved except to be moved out of the hospital.

When a contagious disease occurs in a ward in which the patients are ambulant, all the patients in that ward are considered contacts. In those wards in which all patients are confined to bed, only those children in the room in which the contagious disease occurs are considered contacts.

We have classified the contacts as immune and susceptible rather arbitrarily. Although this division may be questioned, it has been found useful for the purpose of facilitating our procedure. Children who have received intramuscular injections of blood are considered immune for eight days after injection. After eight days have elapsed these children are again considered susceptable.

In brief, the following procedures are used when a contagious disease occurs in a ward:

If measles occurs in a room or ward in which all other children are immune, no quarantine is required. If it occurs where there are susceptible contacts,

measles restrictions are established. No susceptible contact may be moved from the room for sixteen days after exposure, except to be removed from the children's division. Immune patients may be admitted to or removed from the exposed unit, provided passive immunization of the patient and his new contacts is continued. Both immune and susceptible patients are passively reimmunized on the eighth and the sixteenth days. Measles restrictions may be discontinued on the sixteenth day after recognition of the last case of measles. If reexposure occurs more than eight days after the last injection, the procedure must be repeated.

When scarlet fever occurs in the ward a blood agar plate culture of secretion from the nose and throat and a Dick test are made immediately on all contacts, including physicians, nurses and attendants. The culture is repeated the following day. Those persons with negative Dick reactions and two negative cultures are released from quarantine. Those with positive cultures and negative Dick reactions are considered immune but potential sources of infection and are placed in isolation. If a child has a positive culture and a positive Dick reaction, he is considered to be in the early stage of scarlet fever and is transferred to the contagious division. Those children with positive Dick reactions are considered susceptible and receive 10 to 15 cc. of convalescent scarlet fever serum or 20 to 30 cc. of whole blood intramuscularly. Rooms containing contacts are kept closed for a minimum of forty-eight hours. Rooms may be opened at the end of this time, provided every child has had two negative cultures.

When diphtheria occurs in a ward all contacts are quarantined. Cultures of secretion from the nose and throat and Schick tests are made at once on all patients considered as contacts. Similar cultures are made on physicians, nurses and attendants working in the ward and are repeated in twenty-four hours. Children with positive cultures and positive Schick reactions are considered to have diphtheria, are given adequate antitoxin and are transferred to the contagious division. Those who have positive cultures and negative Schick reactions but show no signs of clinical diphtheria are considered carriers and are sent to the contagious division. The room or ward is kept quarantined until the Schick tests and cultures have been read and recorded and all infected patients removed. Children with positive Schick reactions but negative cultures are examined daily for signs of infection. It is in our opinion undesirable to give a prophylactic dose of antitoxin to a clinically normal child with a negative culture. Any exposed child who has a positive Schick reaction and in whom rhinitis, pharyngitis, tonsillitis or laryngitis develops receives antitoxin without our awaiting the result of the culture.

When whooping cough occurs in the ward, all contacts must remain in that ward for two weeks from the time of the occurrence of the last case. All exposed children receive 20 to 40 cc. of whole blood intramuscularly. Administration of pertussis vaccine is begun at once; five injections are given, one every third day. New patients may be admitted to the room or ward if necessary, provided immunization is begun at once.

When chickenpox develops in a ward, the room in which the case occurs is closed for twenty-one days or until all susceptible contacts have been discharged. Control of this disease by quarantine and passive immunization, while appearing to be effective during this period of study, has not proved satisfactory in our past experience.

When mumps occurs, the room in which it appears is closed for twenty-one days or until all susceptible contacts have been discharged. No immunization is attempted except in boys over 10 years of age, who usually receive 10 cc. of mumps convalescent serum or 20 cc. of whole blood intramuscularly.

An arbitrary period of eighteen months, from Dec. 1, 1936 to May 31, 1938, has been chosen for the purpose of analyzing the results. There was a high incidence of measles in the community during this time.

(The incidence of each of the six common contagious diseases diagnosed in the examining room and occurring in the hospital during this time was shown by slides. The data were grouped in three month periods for ease of demonstration.)

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(The incidence of each of the six common contagious diseases diagnosed in the examining room and occurring in the hospital during this time was shown by slides. The data were grouped in three month periods for ease of demonstration.)

During this period of eighteen months 6,080 children were admitted to the hospital. There were 166 cases of contagious disease diagnosed in the examining room. A contagious disease occurred primarily in 63 patients and from these 15 secondary cases were contracted during the stay in the hospital.

With utilization of the routine outlined, contagious diseases have not interfered with the function of the children's division of the Cook County Hospital. At no time was it necessary because of an epidemic within the institution to refuse admission to a single child needing hospitalization.

DISCUSSION

DR. ARCHIBALD L. HOYNE: This subject has been presented in a complete and excellent manner. However, I think one may question the justification for giving whole blood to every patient entering the hospital. I doubt very much if there have been any more cross infections in the Children's Memorial Hospital than in the Cook County Children's Hospital. Furthermore, at the Municipal Contagious Disease Hospital, where cross infections might be expected to occur with greater frequency, I believe the incidence of cross infections due to measles and chickenpox has been no higher than that illustrated on the slides. If children are to be protected by convalescent serum when a contagious disease occurs in the ward, it would appear unnecessary to give blood intramuscularly to every patient who is admitted to the hospital. To do so, it seems, would occasion a great deal of unnecessary work.

DR. MAURICE L. BLATT: The situation in the children's division of the Cook County Hospital is much as Dr. Jacobs has shown on the slides. Large groups of children with various types of infection congregate in one room awaiting diagnosis. They are brought in by the police or the parents. This arrangement is not comparable with that at the Municipal Contagious Disease Hospital, where the patient comes in with a diagnosis and is sent directly to the proper ward. In this children's hospital the child over 2 years of age goes into a cubicle of a room, and if a contagious disease develops in him he exposes all the children in that room. Knowing that the possibility of exposure to cross infection is so great, the type of treatment Dr. Jacobs has outlined has been developed in order to keep all the wards open. We have found that this passive immunization lasts for approximately eight days. When we have failed to reimmunize at the end of that period, in the event of exposure secondary cases have occurred; but when we reinjected whole blood, secondary cases have not occurred.

I do not know what the incidence of infection in the Children's Memorial Hospital is, but in that institution the children are not massed, as they are with us, prior to diagnosis. It is not a lack of realization of the necessity for segregation but the architecture of the building and the large number of patients applying for admission which make isolation impossible. We hope in the next year to be able to admit all children through a cubicle system and so rapidly that contact with persons with contagious diseases will be reduced. It is our opinion that the injection of whole blood is desirable as a means of passive immunization, and its use will be continued in the Cook County Children's Hospital.

DR. E. T. MCENERY: I should like to ask a question with reference to the control of nurses. Dr. Jacobs said that when cases of scarlet fever occur, they perform cultures and Dick tests on all contacts, and if a nurse has a negative Dick reaction and a positive culture she is isolated. That is one difficulty encountered at the Children's Memorial Hospital—nurses with negative reactions to Dick tests and positive throat cultures. Many times a nurse is isolated for five or six weeks before a negative culture is obtained. I wonder how long such nurses are isolated at the Cook County Hospital. At the Children's Memorial Hospital it has been a question as to when they should go back to duty.

Have any accidents occurred in giving whole blood to all of the children who have had contact with persons with these diseases?

DR. MANDEL L. SPIVEK: Have there been any accidents, such as the occurrence of malaria in the case of Greek children? Has there been any transmitted syphilis? I understand the procedure is carried out in the admitting room, using whole blood from the child's parents.

DR. GERARD N. KROST: I should like to know where the large amount of whole blood has been obtained—from the blood bank or from the parents?

DR. NOEL SHAW: I think the figures are impressive. I should like to ask if Dr. Jacobs and Dr. Blatt have any figures on the number of cross infections now as compared with those before such immunization with whole blood was instituted.

DR. H. M. JACOBS: As to whether we should have more contagion with or without the use of whole blood, we have no figures to compare, because we have no records prior to the time we started its use, and it would be an enormous task to compile them. I should like to have a comparison of figures at our institution or any other, to see what would be shown. We do not believe our situation is similar to that in hospitals which have better facilities for isolation in their examining rooms. As reported in the AMERICAN JOURNAL OF DISEASES OF CHILDREN (**57**:322-329 [Feb.] 1939), Barenberg and his co-workers in the Morrisania City Hospital in New York carried out a study of patients admitted to the children's surgical and medical wards. From 1935 to 1937 inclusive they had 12 outbreaks of contagious disease in the surgical ward and none in the medical. In the four years prior to that period they had had 15 outbreaks in the surgical ward and 13 in the medical. They did nothing different except to give parental blood-serum to the children admitted to the medical ward.

So far as the unnecessary work involved in the injection of blood is concerned, all I can say is that we do not mind the work if it does any good.

In reference to Dr. McEnery's query about the negative Dick reaction and the positive culture in exposed nurses, we have the same problem; and it is difficult to clear up the cultures. We do not keep such nurses in the children's division but transfer them to the adult wards, where they will not expose susceptible children.

In answer to Dr. Spivek's question regarding accidents with whole blood, I may say that a number of years ago we had a patient to whom malaria was transferred by injection of whole blood from the father, who had had malaria twenty years previously. We are now using pooled blood from the blood bank, of which examinations, cultures and Wassermann tests have been made. Blood is drawn from the parents and sent to the bank, and an equal amount of tested blood is withdrawn from the bank for use in the wards.

Use of Zinc Peroxide in Infection with Microaerophilic Hemolytic Streptococcus. DR. JOHN S. MCDAVID.

Dr. F. L. Meleney, of New York, has reported some 40 cases of infection caused by an anaerobic hemolytic streptococcus. He described these infections as being slowly progressive and chronic; they spread through subcutaneous tissues by burrowing sinuses that cause liquefaction of fatty tissue and formation of ulcers by the thinning of the skin from beneath. The duration of the condition was from several weeks to several years. Radical resection of the infected area, with the application of a solution of zinc peroxide, was followed by an immediate advantageous response in practically all cases. The organism recovered from the deep-lying secretions was an anaerobic hemolytic streptococcus that grew as an aerobe after a few transplants on artificial mediums. The reaction of the infected tissues was so characteristic and the behavior of the organism so uniform that Dr. Meleney spoke of the infection as a "clinical entity" and called the bacterium a "microaerophilic hemolytic streptococcus." There has been no report of such an infection in a child.

An 8 year old boy was operated on for appendicitis and a gangrenous appendix removed. Four days later, general and local signs of infection appeared, and a

stitch abscess was allowed to drain. However, the infection spread with great rapidity along the fasciae and through the subcutaneous and fatty tissues by the formation of sinuses until large "pockets" of pus developed in the right lumbar region and in the right and left epigastric regions. From cultures of the deep-lying pus an anaerobic hemolytic streptococcus was obtained.

On the eighth postoperative day, the subcutaneous tissues and skin of the left epigastric region and the entire right side and lumbar region were dissected away from the underlying muscular fasciae. The dissection extended to a point 4 inches (10 cm.) beyond the vertebral line. Skin flaps were held back, and the entire area was packed with a 50 per cent solution of zinc peroxide and water. This pasty solution was sealed in with several layers of fine-meshed gauze and zinc oxide ointment, to prevent evaporation. Clinical response of the patient was immediate, with a fall in temperature and diminution of signs of toxicity. The zinc peroxide was washed off in thirty-six hours with a stream of physiologic solution of sodium chloride, and the tissues were in much healthier condition. Two more dressings of zinc peroxide were necessary. These were done with the patient under gas anesthesia, and any new foci of infection were opened and packed with a solution of zinc peroxide. Seven hundred and fifty cubic centimeters of blood and 3,000 cc. of a 5 per cent solution of dextrose were injected intravenously at intervals during the treatment. On the ninth day after the first dressing with zinc peroxide, there were many areas of healthy granulation tissue, no pus was present and anaerobic cultures showed no growth of streptococci. The skin flaps were pulled down and strapped in place with adhesive tape. Healing proceeded uneventfully, and on the twenty-eighth postoperative day the denuded areas were filled in with pinch grafts from the patient's thigh. The child returned home on the thirty-seventh postoperative day.

Zinc peroxide is a soft, white, tasteless powder resembling zinc oxide. When mixed with water to the consistency of 40 per cent cream, it quickly forms a paste, due to bubbles of nascent oxygen. Although not as much oxygen is available immediately as from hydrogen peroxide or sodium perborate, zinc peroxide continues to eliminate oxygen for forty-eight to seventy-two hours after it is mixed with water. Its products of reduction are harmless to granulation tissue, being only zinc oxide and water. Zinc peroxide may be sterilized in a dry heat autoclave by raising the temperature to 140 F. for four hours. The sterilizing process seems to "mobilize" the oxygen, as it is given off more readily after the process of heating.

The use of zinc peroxide in other disorders has been reported: in Vincent's angina, saprophytic invasion of osteomyelitis, rectoanal fistulas, infections with Clostridium welchii and various types of stomatitis. Its usefulness in treating infections of the mouth is enhanced by the fact that zinc peroxide tends to cling to mucous membranes, much as bismuth preparations do, thus leaving "islands" that give off oxygen for a long time.

DISCUSSION

DR. J. H. SKILES: It was a great pleasure to have the privilege of working with Dr. McDavid in reporting this interesting case. The ultimate success is entirely due to Dr. Meleney, who has written so voluminously on this subject. Most of the work in reviving the use of zinc peroxide has been done by him, and I think it shows the necessity for the study of bacteriologic work, especially in connection with surgery. The technic of application and the proper selection of zinc peroxide are well outlined in his articles. When zinc peroxide is shaken up in a test tube with water the mixture becomes foamy from the oxygen liberated. Zinc peroxide is sterilized at 140 F. for two hours and then mixed with equal parts of water to form a creamlike mixture. The margin of the wound is smeared with zinc oxide ointment and the wound itself filled with this paste. Over this, fine mesh gauze is placed, impregnated with zinc oxide ointment or petrolatum.

The chemical reaction seems to be the slow liberation of oxygen, which continues to form hydrogen peroxide for a long time. Dr. Meleney thinks that is the antiseptic factor. Many of these infections have occurred when drainage was instituted; so the insertion of a cigaret drain at the time of operation does not eliminate the hazard.

The patient in the case reported by Dr. McDavid was operated on in the usual way, by a muscle-splitting incision; the appendix was removed, the stump cauterized and inverted and the wound closed without drainage.

Two weeks ago, at the meeting of the American College of Surgeons at Ann Arbor, Mich., Coller suggested the closing of everything but the skin in potentially infected wounds, as the fat is the part of the abdominal wall most susceptible to infection. His method calls for the insertion of skin stitches, but the sutures are not tied. Over the fascial layer and muscle layer is placed gauze impregnated with acriflavine hydrochloride, which he said is used because it shows better in color photographs. The wound is left open for twenty-four hours; at that time there is sufficient drainage from the deep structures to make one feel safe in removing the gauze and tying the sutures. In cases like ours such closure might be an improvement over the present method and might help to avoid infection. Many surgeons are now leaving the appendectomy wound open when the appendix has ruptured. In our case the appendix was not ruptured, but there must have been some of these organisms in the area of the appendix.

Book Reviews

The Center for Research in Child Health and Development, School of Public Health, Harvard University. II. Types, Levels, and Irregularities of Response to a Nursery School Situation of Forty Children Observed, with Special Reference to the Home Environment. Price, $1.25. Pp. 148, with 8 illustrations and 15 tables. Washington: The Society for Research in Child Development, 1939.

A previous report, publication I of the Center for Research in Child Health and Development, Harvard School of Public Health, describes fully the response to and the general plan of the entire research project and the conditions under which the nursery school was conducted. The present report deals primarily with observations made in a nursery school of 40 children, ranging in age from 2 through 4½ years. Striking differences in adaptability, variety of responses, defenses and permanence of adjustment were observed, raising many questions that cannot be answered through a study of 40 children; but the results should be of interest to others working in a larger field.

The group was predominantly Irish and contained no Jews or Negroes. The homes ranged from poor to moderately comfortable, and the intelligence quotients, from 72 to 132. The children attended a nursery school in groups of 5 or 6 at a time for an initial period of from four to six weeks; each group as far as possible returned every six months for an additional observation period of two weeks, until the children reached kindergarten age.

A child's daily activities in the nursery school were of three sorts: routine, directed and undirected. Routine activities, which include care of wraps, routine of toilet, lunch and rest, were recorded on mimeographed forms. Directed activities include story and music periods and group games and were also recorded on mimeographed forms. Records of undirected activities were collected on daily forms and also on a series of timed diary records made under as uniform conditions as possible to give a basis of comparison of the same child at different periods and of one child with another.

Observed responses of the children to their new environment, such as postural tensions, tics, anxious expressions, dreamy watching, rejection of group activities and calls for mother, all decreased with each succeeding week in the nursery; and although on the second visit to the nursery about half of the children showed the same manifestations, they disappeared much more rapidly than at the first visit.

A definite relation was observed between the intelligence quotient and the ability to remember the routine, as measured by the time it took a child to learn the location of his own locker and towel hook. Changes in activities were found to have a definite relation to age.

Three different types of reactions to the new experience of a nursery school are discussed, using changes of activities, materials used, total vocabulary, minutes spent in watching, contacts with children and contacts with adults in classifying the types of adjustment. It was found there were wide differences among the 40 children and that in some instances there were marked contrasts between behavior at the beginning of the observations and at the end. Some children were high in responses at the beginning of the period, with a sharp drop as their visit at the nursery progressed. Some were low at first and became high. Certain children appeared to be consistent in the frequency of their responses. Some children, in a lesser degree, showed a tendency to parallel increase or

decrease in their responses during the course of the visits. Case studies are given to show the individual responses of different children.

On the basis of the responses the children seemed to fall into three groups, accelerated, inhibited and alternating, the last group showing frequent fluctuations. Nervous responses of the three groups are discussed, but with the small number studied they merely show a trend rather than a definite pattern.

The relation of the intelligence quotient to the type of response is interesting, in that among the children with lower intelligence quotients 6 were accelerated, 1 inhibited and 6 alternating, while among the group with the highest intelligence quotients none were accelerated, 8 were inhibited, and 5 alternating, indicating that possibly the child with the high intelligence quotient is more sensitive to a new situation than the child with a low intelligence quotient. It is also of interest to learn that there was a greater incidence of emotionally alternating children when there was a disturbance of health of mother or child or an excessive degree of maternal solicitude.

In addition to observations bearing on types of adjustment to the new environment of a nursery school, there is also a collection of data concerning levels of response at successive age periods. The observation period was sufficiently long to give a reasonably clear picture of each child's capabilities and difficulties at different age periods. Later checks and return visits to the nursery showed the relative gains of each child during the interval.

Interesting studies of the intellectual responses of the children were made. The studies include observation of development of language, recognition of differences in form, matching colors, responses to pictures, block building, use of paints, crayons and clay and rhythmic responses.

Observations of social and emotional responses had to do with attitudes and were harder to define than observations of skills. Social and emotional responses were less definitely related to age levels. Attention was particularly focused on persistent qualities of the individual child as seen apart from the newness of the situation and as carried over from one age to another and from one visit to another. These observations were made after the first reaction to the new environment had subsided. They showed many variations, and many factors entered into the responses of the individual children. The precise significance of variation in these responses is not clear, but the nursery situation is of primary interest as a social situation and of value in research because of the importance of these social and emotional responses.

Many irregularities and inconsistencies were noted in the responses of the children observed. Case histories demonstrate the effect of the home environment and the response of the children to the new environment of the nursery school.

In concluding, it may be well to repeat that the small number of children observed in this study permits of only tentative answers to the questions raised, but the results of such observations should be significant to others working in larger fields.

Die Anachorese ein biologischer Vorgang. By Alberto Ascoli, M.D. No price given. Pp. 165, 4 figures and 72 tables. Milan: Instituto Vaccinogeno Antitubercolare, 1938.

Anachoresis is a Greek word meaning refuge. Ascoli uses the term for the description of a phenomenon which was observed before his time but the practical and multiplex application of which is his own contribution. He observed, in the course of his work on animals with the BCG vaccine of Calmette that a local inflammatory process is a center of attraction for various pathogenic micro-organisms which occur in other parts of the body. After the micro-organisms are drawn to the site of the local inflammation, they are rapidly destroyed. Ascoli uses the term "anachoresis" for this process of attraction and destruction through a focal inflammatory lesion.

Ascoli tried to demonstrate anachoresis clinically, histologically or bacteriologically, using BCG vaccine or other anachoresiogenic micro-organisms, in the following animals with the following bacteria:

1. In newborn calves against the causative organism of septic bronchopneumonia.
2. In rabbits against Bacillus cuniculi septicus.
3. In rabbits and guinea pigs against Bacillus vituli septicus.
4. In mice against streptococci.
5. In guinea pigs against Streptococcus mastitidis.
6. In guinea pigs against Actinobacillus mallei.
7. In calves against Actinomyces.

From these experiments it became obvious that:

1. Several micro-organisms or oil of turpentine can be used for the production of the local abscess.
2. Anachoresis can be demonstrated from two hours to three months after the initial anachoresiogenic injection.
3. Fresh local lesions produce stronger anachoresis than older ones.
4. If a combination of micro-organisms is injected simultaneously, only one of the bacteria may be demonstrated in the anachoretic abscess.
5. Excision of the local lesion terminates the phenomenon of anachoresis.
6. In all experiments, animals which showed anachoresis had milder disease and lived longer than the controls.
8. The pathogenic micro-organisms found in the anachoretic local lesions offer ideal material in vivo for the preparation of specific vaccines.

Ascoli's book shows the highest degree of scientific ingenuity and imagination. His protocols are honestly presented in detail. It seems unfortunate that the number of animals on which each set of experiments was carried out is so small that none of the results can be considered statistically significant. The book offers many interesting ideas with the possibility of important practical application. It would be well worth while to repeat Ascoli's experiments on statistically significant numbers of animals.

School Health Problems. By Drs. Laurence B. Chenoweth and Theodore K. Selkirk. Second edition. Price, $3.00. Pp. 419, with 115 illustrations. New York: F. S. Crofts and Company, 1940.

This book is a revision of the useful text published in 1937 and reviewed in this journal. It is particularly recommended for students of education and teachers in service. The compilation of materials on growth, nutrition and other factors concerned with the health of the school child makes it useful as well for nurses and other students of public health.

The revision is not extensive but brings the material up to date or improves it. There are 12 added pages on "Sanitation of the School," a brief chapter on "The Teaching of Health" and appendixes: "Quarantine Regulations" and "Reading Disability."

Public education should help to extend the medical supervision of health by the pediatrician, but to achieve this there must be more understanding of health problems by teachers and school administrators. The material discussed in this text should be useful in clearing up much of the lack of comprehension of health problems, but it is not adequate for clarifying the problems of particular interest to school administrators. School superintendents and principals are often without understanding of the relative values of different aspects of the health program, and yet they may be responsible for making decisions as to how the physician and other members of the health supervision personnel must spend their time.

What is described as a modern and up-to-date program for "prevention of tuberculosis" seems likely to be misleading to educational administrators. The authors quote figures collected about Philadelphia to imply that 12 per cent of children need careful supervision and follow-up for the prevention of active tuberculosis in the future. Following many roentgen findings, special studies, such as those made at Phipps Institute, may appropriately be carried out over an extended period for research purposes, but not all tuberculosis experts would agree that the whole program given on pages 267 and 268 is practical under present conditions or that it should have precedence over the more important efforts to discover cases of tuberculosis among the adult population. Such a thorough and intensive program should be decided on after the budget of the whole community has been considered. The school health budget should have balance and should be planned along with the public health budget. Opportunism may be justified in some instances, but leaders in public health should attempt to develop the most productive services without expending too large a proportion of the budget on activities that yield low returns per unit cost.

Bacillaire dysenterie bij kinderen te Batavia. By B. Lammerts Van Bueren. Price, none given. Pp. 204, with 11 illustrations. Batavia: Olt and Company, 1939.

Bacillary dysentery has long been one of the most frequently encountered infectious diseases among children of all national groups in the Netherland East Indies. This study is based on four hundred observations made in the children's wards of the General Civil Hospital in Batavia during the period from 1935 to 1937. The larger percentage of patients were native or Chinese, although children of European parents represented 12 per cent of the total. The most constant symptoms were high fever and presence of mucus and some blood in the stools, which were not watery for the most part. Intoxication and death were much more frequent in infants and children in a poor state of nutrition at the onset of the disease. For bacteriologic confirmation it was found important to examine three or more consecutive specimens within the first few days of the disease because of the frequency with which examination of a single stool gave a negative result. Of the 296 cases in which the diagnosis was bacteriologically confirmed, in about 70 per cent the organism belonged to the Y Flexner group, in 20 per cent to the Sonne group and in 1 to 5 per cent to the Shiga group, while in 5 to 10 per cent there was a mixed infection. The severity of the disease did not bear any direct relation to the type of infecting organism but was rather a reflection of the general condition of the child.

The mortality for infants was about 50 per cent and that for older children 35 per cent. The time of year had no demonstrable influence on the incidence of the disease. Observations at autopsy were similar to those reported in other countries. Occasionally positive cultures were obtained from autopsy material in cases in which cultures had been negative during life. It is thought that the incubation period is from a few hours to two days, and apparently an attack of bacillary dysentery confers on children no immunity or one of short duration only. Much needs still to be done in improvement of sanitary conditions and regulations in order to decrease the scourge of this disease in the Netherland East Indies.

Clinique et physiopathologie des maladies coeliaques. By Robert Dubois. Price, 80 francs. Pp. 350, with 14 illustrations. Paris: Masson & Cie, 1939.

The experimental work of Versar in producing a condition resembling celiac disease in animals by poisoning with monoiodoacetic acid gave impetus to this clinical study of celiac disease in children and of nontropical sprue in adults. Versar found that his poisoned animals lost the power of absorption of some substances. This loss involved absorption of fats and the products of their digestion, dextrose and galactose. Other sugars and proteins were absorbed normally. The same selective impairment of absorption was found to exist in the patients

studied by Dubois. Disturbances of mineral, water and vitamin absorption seem to be secondary rather than primary, with the exception of impaired absorption of riboflavin (vitamin G, or B_2). Phosphorylation of riboflavin occurs normally in the intestinal mucosa and is a prerequisite for absorption. This process is definitely impaired both in poisoned animals and in human beings with celiac disease or with nontropical sprue. Since riboflavin is particularly a growth vitamin, the author feels that its lack is responsible for the infantilism and dwarfing in celiac disease. Versar was also able to produce a picture similar to that obtained with monoiodoacetic acid by adrenalectomy and by depriving his animals of riboflavin. The picture produced by all three procedures could be converted to normal by administration of phosphorylated riboflavin.

The cause of the impaired selective absorption in human patients is not clear. Dubois could find no definite evidence of adrenal disturbance. Phosphorylated riboflavin is not yet obtainable in sufficient quantities to determine its curative effect on human beings, although there are a few enthusiastic reports of recovery following the use of liver extract parenterally.

The rationale both of Fanconi's fruit diet and of a high protein diet is easily understood in the light of these findings. The practical role of the phosphorylated form of vitamin B_2 may be determined in the near future.

Dubois is to be congratulated on his clinical studies and on the sound and stimulating presentation of his subject.

Essentials of the Diagnostic Examination. By Dr. John B. Youmans. Price, $3.00. Pp. 417, with 36 illustrations and 23 tables. New York: The Commonwealth Fund, 1940.

This is a short, concise and practical manual for the general practitioner. There are three parts, dealing with history and physical examination, laboratory tests and miscellaneous tests. In general, no attempt is made to provide a physiologic background or to enter into detailed or theoretic discussions. The subject matter has been reduced to its simplest form.

The first section is especially well done. The author has managed to condense most of the meat of much larger volumes into only 156 pages. Several good charts regarding the distribution and function of various parts of the nervous system are included. The second section describes the ordinary laboratory procedures and their significance. Alternative methods are not given for the most part. This section is relatively complete, including, for example, procedures for typing of pneumococci, examination of spinal fluid (with an excellent chart of findings in different conditions), simple blood chemistry and skin tests, as well as examination of blood, urine and feces. Procedures are adequately described and interpretations briefly discussed. Under miscellaneous tests are taken up a few, more difficult blood analyses, agglutination tests, the Wassermann test, etc. Included in the appendix is a description of the equipment necessary for a small office laboratory.

This book should fill a real need, especially for the physician who has to rely entirely on his own laboratory for information or is located in a small town.

Précis de médecine des enfants. By P. Nobécourt. Sixth edition. Price, 175 francs. Pp. 1,304, with 604 illustrations. Paris: Masson & Cie, 1939.

This is the sixth edition of a well known text written by one of the world's authorities in pediatrics. It is well got up; the illustrations are ample, and the typography is such that it is not hard for the reader to pick out the important points on a subject.

There is no attempt to quote the literature, but the whole book is a most creditable presentation of clinical pediatrics. One objection to the book, which is true of practically all French texts, is that, while it has an ample table of contents, there is no index.

Directory of Pediatric Societies*

INTERNATIONAL

International Association of Preventive Pediatrics

President: Prof. S. Monrad, Dronning Louises Børnehospital, Copenhagen, Denmark.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

International Congress of Pediatrics

American Committee:

Chairman: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
General Secretary: Dr. Kenneth D. Blackfan, 300 Longwood Ave., Boston.
Assistant Secretary-Treasurer: Dr. Charles F. McKhann, 300 Longwood Ave., Boston.

Canadian Committee:

Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto.
Secretary: Dr. H. P. Wright, 1509 Sherbrooke St. W., Montreal.
Place: Boston, Mass. Time: Postponed indefinitely.

International Congress for the Protection of Infancy

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.

FOREIGN

Argentine Pediatric Society of Buenos Aires

President: Dr. Martin Ramón Arana, 1809 Rodriguez Peña, Buenos Aires.
General Secretary: Dr. Alfredo Larguia, Cerrito 1179, Buenos Aires.

British Paediatric Association

President: Prof. Charles McNeil, 44 Heriot Row, Edinburgh, Scotland.
Secretary: Dr. Arthur G. Maitland Jones, 31A Weymouth St., London, W. 1.

Danish Pediatric Society

President: Dr. E. Lenstrup, Copenhagen.
Secretary: Dr. E. Gjørup, Dronning Louises Børnehospital, Copenhagen.

Paediatrický Spolok na Slovensku

President: Dr. A. J. C. Chura, Lazaretská 11, Bratislava.
Secretary: Dr. P. Rados, Lazaretská 6, Bratislava.
Place: Pediatric Clinic, University Bratislava. Time: Six times a year.

Royal Society of Medicine, Section for the Study of Disease in Children

President: Dr. E. A. Cockayne, 98 Harley St., London, W. 1, England.
Secretary: Dr. R. Lightwood, 86 Brook St., London, W. 1, England.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:15 p. m.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

PALESTINE JEWISH MEDICAL ASSOCIATION, SECTION OF PHYSICIANS OF CHILDREN'S DISEASES

President: Prof. S. Rosenbaum, 26 Bialikstr., Tel Aviv.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv.

SOCIEDAD CUBANA DE PEDIATRÍA

President: Dr. Clemente Inclan Costa, Manrique 48, Habana.
Secretary: Dr. Serafin Falcon Lopez, Calle B No. 356, Vedado, Habana.
Place: Cátedra de Clinica Infantil, Hospital Mercedes, Habana. Time: Last Wednesday of every month.

SOCIEDAD MEXICANA DE PEDIATRIA

President: Dr. Jorge Muñoz Turnbull, Av. Alvaro Obregón 186, Mexico, D. F.
Secretary: Dr. Fernando López Clares, Medellín 191, Mexico, D. F.

SOCIÉTÉ DE PÉDIATRIE DE PARIS

President: Dr. B. Weill-Hallé, 49 Avenue Raymond Poincaré, Paris, France.
Secretary: Dr. Jean Hallé, 10 bis Rue du Pré aux Clercs, Paris, France.
Place: Hôpital des Enfants Malades, 49 Rue de Sèvres. Time: 4:30 p. m., third Thursday of every month.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON PEDIATRICS

Chairman: Dr. Julius H. Hess, 104 S. Michigan Ave., Chicago.
Secretary: Dr. Hugh L. Dwyer, 315 Alameda Rd., Kansas City, Mo.
Place: Cleveland.

AMERICAN ACADEMY OF PEDIATRICS

President: Dr. J. B. Bilderback, 1020 S. W. Taylor St., Portland, Ore.
Secretary: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.
Place: Hotel Peabody, Memphis, Tenn. Time: Nov. 18-20, 1940.
Region I. Place: New Haven, Conn. Time: March 27-29, 1941.
Region II. Place: Richmond, Va.
Region III. Place: Palmer House, Chicago. Time: May 15-17, 1941.
Region IV. Place: San Francisco.

NORTHERN CALIFORNIA AFFILIATES

President: Dr. Crawford Bost, 490 Post St., San Francisco.
Secretary: Dr. William A. Reilly, 384 Post St., San Francisco.
Time: Second Thursday of September, November, January, March and May.

AMERICAN HOSPITAL ASSOCIATION, CHILDREN'S HOSPITAL SECTION

Chairman: Dr. D. L. Richardson, 593 Eddy St., Providence, R. I.
Secretary: Dr. Joelle C. Hiebert, 299 Main St., Lewiston, Maine.

AMERICAN PEDIATRIC SOCIETY

President: Dr. Thomas B. Cooley, 1728 Seminole Ave., Detroit.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid Ave., St. Louis.
Place: Hot Springs, Va. Time: May 22-24, 1941.

CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

President: Dr. L. M. Lindsay, 815 Medical Arts Bldg., Montreal.
Secretary-Treasurer: Dr. Elizabeth Chant Robertson, Hospital for Sick Children, Toronto.

Society for Pediatric Research

President: Dr. A. Ashley Weech, 3975 Broadway, New York.
Secretary: Dr. Mitchell I. Rubin, 1740 Bainbridge St., Philadelphia.

SECTIONAL

Intermountain Pediatric Society

President: Dr. Eugene Smith, 385–24th St., Ogden, Utah.
Secretary-Treasurer: Dr. W. C. Cheney, 837 Boston Bldg., Salt Lake City.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

New England Pediatric Society

President: Dr. R. Cannon Eley, 319 Longwood Ave., Boston.
Secretary-Treasurer: Dr. James Marvin Baty, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

North Pacific Pediatric Society

President: Dr. S. G. Henricke, 4215 N. E. Hancock St., Portland, Ore.
Secretary: Dr. J. S. Backstrand, 388 State St., Salem, Ore.

Rocky Mountain Pediatric Society

President: Dr. Donn Barber, 802½–8th Ave., Greeley, Colo.
Secretary: Dr. Kenneth Schmidt, Republic Bldg., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 7:30 p. m.

Southern Medical Association, Section of Pediatrics

Chairman: Dr. Harvey F. Garrison, 319 E. Capitol St., Jackson, Miss.
Secretary: Dr. Warren W. Quillian, 227 Aragon Ave., Coral Gables, Fla.
Place: Louisville Ky. Time: Nov. 12-15, 1940.

STATE

Alabama Pediatric Society

President: Dr. Stewart H. Welch, 1117 S. 20th St., Birmingham.
Secretary-Treasurer: Dr. William R. Britton, 4 Catoma St., Montgomery.
Place: Birmingham. Time: Sept. 18, 1940.

Arkansas State Pediatric Association

Chairman: Dr. C. B. Billingsley, 1425 N. 11th St., Fort Smith.
Secretary: Dr. R. E. Weddington, 1425 N. 11th St., Fort Smith.

California State Medical Society, Section on Pediatrics

Chairman: Dr. William Belford, 233 A St., San Diego.
Secretary: Dr. Louis M. Earle, 6381 Hollywood, Hollywood, Calif.
Place: Del Monte. Time: May 1941.

Florida State Pediatric Society

President: Dr. Warren W. Quillian, 227 Aragon Ave., Coral Gables.
Secretary: Dr. George N. Leonard, 605 Lincoln Rd., Miami Beach.
Place: Concurrent with state association meeting at time of convention.

Georgia Pediatric Society

President: Dr. R. C. McGahee, 1345 Greene St., Augusta.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.

Hezekiah Beardsley Pediatric Club of Connecticut

President: Dr. Oliver L. Stringfield, 1416 Bedford St., Stamford.
Secretary: Dr. Joseph L. Hetzel, 103 N. Main St., Waterbury.
Time: Three meetings a year.

Illinois State Medical Society, Section on Pediatrics

Chairman: Dr. Orville Barbour, 331 Fulton St., Peoria.
Secretary: Dr. Craig Butler, 715 Lake St., Oak Park.
Place: Chicago. Time: May 1941.

Indiana State Pediatric Society

President: Dr. K. T. Knode, 1105 E. Jefferson Blvd., South Bend.
Secretary-Treasurer: Dr. Mathew Winters, 621 Hume Mansur Bldg., Indianapolis.
Time: Two meetings a year.

Iowa Pediatric Society

President: Dr. Morgan J. Foster, 837 Higley Bldg., Cedar Rapids.
Secretary-Treasurer: Dr. Arnold M. Smythe, 406–6th Ave., Des Moines.

Louisiana State Pediatric Society

President: Dr. H. Aubrey White, Alexandria.
Secretary-Treasurer: Dr. W. C. Rivenbark, 3503 Prytania St., New Orleans.
Place: Shreveport. Time: April 1941.

Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. Norman L. Hawkins, 11 Public Sq., Watertown, N. Y.
Secretary: Dr. William J. Orr, 135 Linwood Ave., Buffalo.

Medical Society of the State of Pennsylvania, Pediatric Section

Chairman: Dr. Ralph M. Tyson, 255 S. 17th St., Philadelphia.
Secretary: Dr. John D. Sturgeon Jr., 22 N. Gallatin Ave., Uniontown.
Place: Philadelphia, Pa. Time: Sept. 30-Oct. 3, 1940.

Michigan State Medical Society, Pediatric Section

President: Dr. Ward L. Chadwick, 524 Medical Arts Bldg., Grand Rapids.
Chairman: Dr. Harry Towsley, University of Michigan Hospital, Ann Arbor.
Place: Detroit. Time: Sept. 25-27, 1940.

Mississippi State Pediatric Society

President: Dr. Guy C. Jarratt, 920 Crawford St., Vicksburg.
Secretary-Treasurer: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Place: To be designated by society. Time: Yearly.

Nebraska Pediatric Society

President: Dr. Herman M. Jahr, 1120 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. Elmer W. Bantin, 440 Aquila Court Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

North Carolina Pediatric Society

President: Dr. Marion Y. Keith, 369 N. Elm St., Greensboro.
Secretary: Dr. G. W. Kutscher Jr., 176 Woodfin St., Asheville.

Oklahoma State Pediatric Society

President: Dr. J. B. Snow, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. G. R. Felts, 1200 N. Walker St., Oklahoma City.
Place: Oklahoma Club. Time: 6:30 p. m., fourth Friday of each alternate month from September to May, inclusive.

South Carolina Pediatric Society

President: Dr. R. B. Josey, 1517 Hampton Ave., Columbia.
Secretary-Treasurer: Dr. Wilson Ball, South Carolina State Health Dept., Columbia.

Tennessee State Pediatric Society

President: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis.
Secretary: Dr. Gilbert Eblen, 607 Medical Arts Bldg., Knoxville.

Texas Pediatric Society

President: Dr. C. P. Jasperson, 509 Nixon Bldg., Corpus Christi.
Secretary-Treasurer: Dr. F. H. Lancaster, 4409 Fannin St., Houston.
Place: Galveston. Time: Oct. 5, 1940.

Virginia Pediatric Society

President: Dr. S. A. Anderson Jr., 2326 W. Grace St., Richmond.
Secretary: Dr. John M. Bishop, 511 Medical Arts Bldg., Roanoke.
Place: White Sulphur Springs, W. Va. Time: July 24, 1940.

West Virginia State Medical Society, Section on Pediatrics

President: Dr. Raymond Sloan, 1139–4th Ave., Huntington.
Secretary: Dr. Thomas G. Folsom, 1139–4th Ave., Huntington.
Place: White Sulphur Springs. Time: July 29-31, 1940.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. J. D. Nourse, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. I. B. Silber, 10465 Carnegie Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. T. B. Verner, 170 St. George St., Toronto, Canada.
Secretary: Dr. D. V. Hutton, 170 St. George St., Toronto, Canada.

Bronx Pediatric Society

President: Dr. Harry S. Altman, 940 Grand Concourse, New York.
Secretary: Dr. David Zahn, 2474 Valentine Ave., New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

Brooklyn Academy of Pediatrics

President: Dr. Archibald Smith, Garden City, N. Y.
Secretary: Dr. Walter Coles, 604–2d St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Fourth Wednesday of each month, except May, June, July, August and September.

Central New York Pediatric Club

President: Dr. Frank van der Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Third Tuesday of April and September.

Chicago Pediatric Society

President: Dr. Gerard N. Krost, 2376 E. 71st St., Chicago.
Secretary: Dr. George F. Munns, 723 Elm St., Winnetka, Ill.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May, inclusive.

Dallas Pediatric Society

President: Dr. Edgar Loomis, 351 W. Jefferson Ave., Dallas, Texas.
Secretary-Treasurer: Dr. John E. Ashby, 3610 Fairmont Ave., Dallas, Texas.
Place: Bradford Baby Hospital. Time: 1 p. m., second and fourth Saturdays of each month.

Detroit Pediatric Society

President: Dr. Robert J. Mason, Birmingham, Mich.
Secretary: Dr. J. Hugh Lewis, 2966 Biddle, Wyandotte, Mich.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month from October to June, inclusive.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. Stephen C. Redd, 157 Forrest Ave. N. E., Atlanta.
Secretary: Dr. C. Dixon Fowler, Medical Arts Bldg., Atlanta.
Place: Academy of Medicine, 38 Prescott St. N. E. Time: Second Thursday of each month from October to April, 8 p. m.

Houston Pediatric Society

President: Dr. Thomas J. Donovan, 3820 Fannin St., Houston, Texas.
Secretary: Dr. Raymond Cohen, 2300 Caroline St., Houston, Texas.
Place: Houston Club. Time: Third Monday of each month.

Kansas City (Missouri) Pediatric Society

President: Dr. John Aull, 1103 Grand Ave., Kansas City.
Secretary: Dr. George Herrman, 1107 Bryant Bldg., Kansas City.
Place: Kansas City General Hospital. Time: On call.

Los Angeles County Medical Association, Pediatric Section

President: Dr. H. R. Cooder, 3875 Wilshire Blvd., Los Angeles.
Secretary-Treasurer: Dr. Paul M. Hamilton, 248 E. Main St., Alhambra, Calif.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd. Time: Second Monday of February, April, June, October and December.

Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Sydney Nussbaum, 247 Ocean View Ave., Brooklyn.
Secretary: Dr. Harry Bikoff, 850 St. Marks Ave., Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: 9:00 p. m., second Monday of each month, October to March, inclusive.

Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. A. A. Trivilino, 88-07–150th St., Jamaica, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144–38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

Medical Society of the District of Columbia, Section on Pediatrics

President: Dr. Harry A. Ong, 1801 I St. N. W., Washington, D. C.
Secretary-Treasurer: Dr. William F. Burdick, 5402 Connecticut Ave. N. W., Washington, D. C.
Place: Medical Society Bldg., 1718 M St. N. W. Time: 8 p. m., fourth Thursday of every month.

Memphis Pediatric Society

President: Dr. E. C. Mitchell, 1073 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Harry Jacobson, 1193 Madison Ave., Memphis, Tenn.
Place: John Gaston Hospital. Time: Quarterly.

Milwaukee Pediatric Society

President: Dr. S. F. Morgan, 2577 N. Downer Ave., Milwaukee.
Secretary-Treasurer: Dr. F. R. Janney, 1411 Wauwatosa Ave., Wauwatosa, Wis.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Leslie O. Ashton, 850 Park Ave., New York.
Secretary: Dr. Alfred Langmann, 108 E. 68th St., New York.
Place: New York Academy of Medicine, 2 E. 103 St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northwestern Pediatric Society

President: Dr. Roland E. Nutting, 205 W. 2d St., Duluth, Minn.
Secretary-Treasurer: Dr. John M. Adams, 1009 Nicollet Ave., Minneapolis.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

Oklahoma City Pediatric Society

President: Dr. J. Byron Snow, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. G. R. Felts, 1200 N. Walker St., Oklahoma City.
Place: Oklahoma Club. Time: Third Friday of each alternate month.

Philadelphia Pediatric Society

President: Dr. Pascal F. Lucchesi, 4000 N. Front St., Philadelphia.
Secretary: Dr. Aims C. McGuinness, Children's Hospital, 1740 Bainbridge St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to April, inclusive.

Pittsburgh Pediatric Society

President: Dr. E. L. Piper, 3200–5th Ave., Pittsburgh.
Secretary-Treasurer: Dr. Carl Ruder, 646 Washington Rd., Mount Lebanon, Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate month from October to June, inclusive.

Richmond Pediatric Society

President: Dr. Charles L. Outland, 312 N. 9th St., Richmond, Va.
Secretary-Treasurer: Dr. T. Stanley Meade, 913 Floyd Ave., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: 8 p. m., third Thursday of each month, except June, July and August.

Rochester Pediatric Society

President: Dr. David Wolin, 16 N. Goodman St., Rochester, N. Y.
Secretary: Dr. W. L. Bradford, 16 N. Goodman St., Rochester, N. Y.
Place: Rochester Academy of Medicine or arrangement by program committee. Time: Third Friday of each month from October to May.

St. Louis Pediatric Society

President: Dr. Max Deutch, 634 N. Grand Blvd., St. Louis.
Secretary-Treasurer: Dr. Peter G. Danis, 634 N. Grand Blvd., St. Louis.
Place: St. Louis Medical Society Bldg. Time: First Friday of each month from October to June.

Seattle Pediatric Society

President: Dr. Jay I. Durand, 1305–4th Ave., Seattle.
Secretary: Dr. Frederick B. Joy, 1215–4th Ave., Seattle.
Place: College Club. Time: Third Friday of each month, 6:30 p. m.

Southwestern Pediatric Society

President: Dr. Norman Nixon, 1136 W. 6th St., Los Angeles.
Secretary: Dr. Donald C. Shelby, 3780 Wilshire Blvd., Los Angeles.
Place: Jonathan Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Mark Osterlin, Central Michigan Children's Clinic, Traverse City, Mich.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.
Time: Nov. 15-16, 1940.

Westchester County Medical Society, Pediatric Section (New York)

President: Dr. M. Bernard Brahdy, 531 E. Lincoln Ave., Mount Vernon.
Secretary-Treasurer: Dr. Elvira Ostlund, 64 Highland Ave., Rye.
Place: Grasslands Hospital, Valhalla, N. Y. Time: Third Thursday in October, December, February and April.